

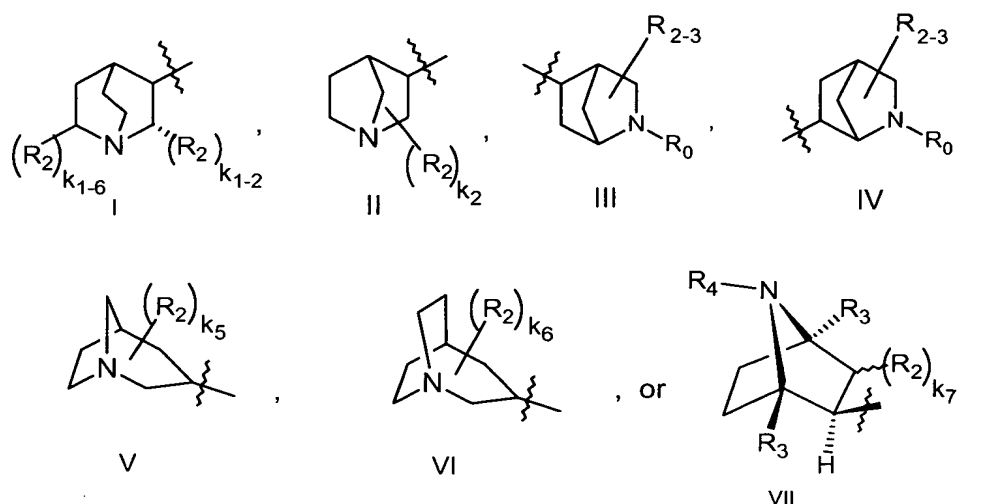
Claims:

1. A method to treat disease or disorder involving cholinergic hypofunction in a mammal in need thereof administering an effective amount of an $\alpha 7$ nAChR full agonist over an effective therapeutic interval with at least one inhibitor, wherein the inhibitor is a beta secretase inhibitor, an acetylcholinesterase inhibitor, and a gamma secretase inhibitor.
2. The method of claim 1, wherein the Acetylcholinesterase inhibitor is physostigmine, aricept, rivastigmine, galantamine, monoamine acridines and derivatives, piperidinyl-alkanoyl heterocyclic compounds, N-benzyl-piperidine derivatives, 4-(1-benzylpiperidyl)-substituted fused quinoline derivatives, and cyclic amide derivatives.
3. The method of claim 1, wherein the disease or condition is cognitive and attention deficit symptoms of Alzheimer's, neurodegeneration associated with diseases such as Alzheimer's disease, pre-senile dementia (mild cognitive impairment), senile dementia, amyotrophic lateral sclerosis, traumatic brain injury, behavioral and cognitive problems in general and associated with brain tumors, AIDS dementia complex, dementia associated with Down's syndrome, dementia associated with Lewy Bodies, Huntington's disease, Parkinson's disease, age-related macular degeneration.
4. The method of claim 1, wherein the mammal is a human.
5. The method of claim 1, wherein the alpha 7 nAChR full agonist is a compound of Formula I:



Formula I

wherein Azabicyclo is



wherein X is O, or S;

R_0 is H, lower alkyl, substituted lower alkyl, or lower haloalkyl;

Each R_1 is H, alkyl, cycloalkyl, haloalkyl, substituted phenyl, or substituted naphthyl;

Each R_2 is independently F, Cl, Br, I, alkyl, substituted alkyl, haloalkyl, cycloalkyl, aryl, or R_2 is absent provided that k_{1-2} , k_{1-6} , k_2 , k_5 , k_6 , or k_7 is 0;

k_{1-2} is 0 or 1;

k_{1-6} is 0 or 1, provided that the sum of k_{1-2} and k_{1-6} is one;

k_2 is 0 or 1;

k_5 is 0, 1, or 2;

k_6 is 0, 1, or 2;

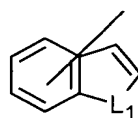
k_7 is 0 or 1;

R_{2-3} is H, F, Cl, Br, I, alkyl, haloalkyl, substituted alkyl, cycloalkyl, or aryl;

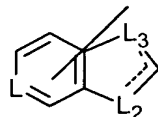
Each R_3 is independently H, alkyl, or substituted alkyl;

R_4 is H, alkyl, an amino protecting group, or an alkyl group having 1-3 substituents selected from F, Cl, Br, I, -OH, -CN, -NH₂, -NH(alkyl), or -N(alkyl)₂;

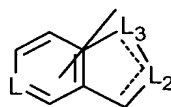
R_5 is 5-membered heteroaromatic mono-cyclic moieties containing within the ring 1-3 heteroatoms independently selected from the group consisting of -O-, =N-, -N(R_{10})-, and -S-, and having 0-1 substituent selected from R_9 and further having 0-3 substituents independently selected from F, Cl, Br, or I, or R_5 is 9-membered fused-ring moieties having a 6-membered ring fused to a 5-membered ring and having the formula



wherein L_1 is O, S, or NR_{10} ,



wherein L is CR_{12} or N, L_2 and L_3 are independently selected from CR_{12} , $C(R_{12})_2$, O, S, N, or NR_{10} , provided that both L_2 and L_3 are not simultaneously O, simultaneously S, or simultaneously O and S, or



wherein L is CR_{12} or N, and L_2 and L_3 are independently selected from CR_{12} , O, S, N, or NR_{10} , and each 9-membered fused-ring moiety having 0-1 substituent selected from R_9 and further having 0-3 substituent(s) independently selected from F, Cl, Br, or I, wherein the R_5 moiety attaches to other substituents as defined in formula I at any position as valency allows;

R_6 is 6-membered heteroaromatic mono-cyclic moieties containing within the ring 1-3 heteroatoms selected from =N- and having 0-1 substituent selected from R_9 and 0-3 substituent(s) independently selected from F, Cl, Br, or I, or R_6 is 10-membered heteroaromatic bi-cyclic moieties containing within one or both rings 1-3 heteroatoms selected from =N-, including, but not limited to, quinolinyl or isoquinolinyl, each 10-membered fused-ring moiety having 0-1 substituent selected from R_9 and 0-3 substituent(s) independently selected from F, Cl, Br, or I, wherein the R_6 moiety attaches to other substituents as defined in formula I at any position as valency allows;

R_7 is alkyl, substituted alkyl, haloalkyl, $-OR_{11}$, $-CN$, $-NO_2$, $-N(R_8)_2$;

Each R_8 is independently H, alkyl, cycloalkyl, heterocycloalkyl, alkyl substituted with 1 substituent selected from R_{13} , cycloalkyl substituted with 1 substituent selected from R_{13} , heterocycloalkyl substituted with 1 substituent selected from R_{13} , haloalkyl, halocycloalkyl, haloheterocycloalkyl, phenyl, or substituted phenyl;

R_9 is alkyl, cycloalkyl, heterocycloalkyl, haloalkyl, halocycloalkyl, haloheterocycloalkyl, $-OR_{14}$, $-SR_{14}$, $-N(R_{14})_2$, $-C(O)R_{14}$, $-C(O)N(R_{14})_2$, $-CN$, $-NR_{14}C(O)R_{14}$, $-S(O)_2N(R_{14})_2$, $-NR_{14}S(O)_2R_{14}$, $-NO_2$, alkyl substituted with 1-4 substituent(s) independently selected from F, Cl, Br, I, or R_{13} , cycloalkyl substituted with 1-4 substituent(s) independently selected from F, Cl, Br, I, or R_{13} , or heterocycloalkyl substituted with 1-4 substituent(s) independently selected from F, Cl, Br, I, or R_{13} ;

R_{10} is H, alkyl, haloalkyl, substituted alkyl, cycloalkyl, halocycloalkyl, substituted cycloalkyl, phenyl, or phenyl having 1 substituent selected from R_7 and further having 0-3 substituents independently selected from F, Cl, Br, or I;

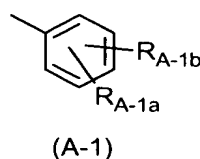
Each R_{11} is independently H, alkyl, cycloalkyl, heterocycloalkyl, haloalkyl, halocycloalkyl, or haloheterocycloalkyl;

Each R_{12} is independently H, F, Cl, Br, I, alkyl, cycloalkyl, heterocycloalkyl, haloalkyl, halocycloalkyl, haloheterocycloalkyl, substituted alkyl, substituted cycloalkyl, substituted heterocycloalkyl, $-CN$, $-NO_2$, $-OR_{14}$, $-SR_{14}$, $-N(R_{14})_2$, $-C(O)R_{14}$, $-C(O)N(R_{14})_2$, $-NR_{14}C(O)R_{14}$, $-S(O)_2N(R_{14})_2$, $-NR_{14}S(O)_2R_{14}$, or a bond directly or indirectly attached to the core molecule, provided that there is only one said bond to the core molecule within the 9-membered fused-ring moiety, further provided that where valency allows the fused-ring moiety has 0-1 substituent selected from alkyl, cycloalkyl, heterocycloalkyl, haloalkyl, halocycloalkyl, haloheterocycloalkyl, substituted alkyl, substituted cycloalkyl, substituted heterocycloalkyl, $-OR_{14}$, $-SR_{14}$, $-N(R_{14})_2$, $-C(O)R_{14}$, $-NO_2$, $-C(O)N(R_{14})_2$, $-CN$, $-NR_{14}C(O)R_{14}$, $-S(O)_2N(R_{14})_2$, or $-NR_{14}S(O)_2R_{14}$, and further provided that the fused-ring moiety has 0-3 substituent(s) selected from F, Cl, Br, or I;

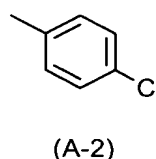
R_{13} is $-OR_{14}$, $-SR_{14}$, $-N(R_{14})_2$, $-C(O)R_{14}$, $-C(O)N(R_{14})_2$, $-CN$, $-CF_3$, $-NR_{14}C(O)R_{14}$, $-S(O)_2N(R_{14})_2$, $-NR_{14}S(O)_2R_{14}$, or $-NO_2$;

Each R_{14} is independently H, alkyl, cycloalkyl, heterocycloalkyl, haloalkyl, halocycloalkyl, or haloheterocycloalkyl;

wherein W is (A):



or



wherein R_{A-1a} is H, alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, haloalkyl, haloalkenyl, haloalkynyl, halocycloalkyl, haloheterocycloalkyl, substituted alkyl, substituted alkenyl, substituted alkynyl, substituted cycloalkyl, substituted heterocycloalkyl, aryl, $-R_5$, R_6 , $-OR_{A-3}$, $-OR_{A-4}$, $-SR_{A-3}$, F, Cl, Br, I, $-N(R_{A-3})_2$,
 5 $-N(R_{A-5})_2$, $-C(O)R_{A-3}$, $-C(O)R_{A-5}$, $-CN$, $-C(O)N(R_{A-3})_2$, $-C(O)N(R_{A-6})_2$,
 $-NR_{A-3}C(O)R_{A-3}$, $-S(O)R_{A-3}$, $-OS(O)_2R_{A-3}$, $-NR_{A-3}S(O)_2R_{A-3}$, $-NO_2$, and
 $-N(H)C(O)N(H)R_{A-3}$;

R_{A-1b} is $-O-R_{A-3}$, $-S-R_{A-3}$, $-S(O)-R_{A-3}$, $-C(O)-R_{A-7}$, and alkyl substituted on the
 ω carbon with R_{A-7} ;

10 Each R_{A-3} is independently selected from H, alkyl, haloalkyl, substituted alkyl, cycloalkyl, halocycloalkyl, substituted cycloalkyl, heterocycloalkyl, haloheterocycloalkyl, substituted heterocycloalkyl, R_5 , R_6 , phenyl, or substituted phenyl;

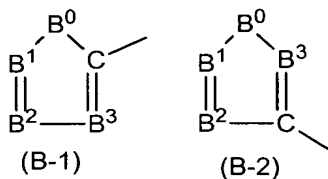
R_{A-4} is selected from cycloalkyl, halocycloalkyl, substituted cycloalkyl, heterocycloalkyl, haloheterocycloalkyl, or substituted heterocycloalkyl;

15 Each R_{A-5} is independently selected from cycloalkyl, halocycloalkyl, substituted cycloalkyl, heterocycloalkyl, haloheterocycloalkyl, substituted heterocycloalkyl, R_5 , R_6 , phenyl, or substituted phenyl;

Each R_{A-6} is independently selected from alkyl, haloalkyl, substituted alkyl, cycloalkyl, halocycloalkyl, substituted cycloalkyl, heterocycloalkyl, halohetero-
 20 cycloalkyl, substituted heterocycloalkyl, R_5 , R_6 , phenyl, or substituted phenyl;

R_{A-7} is selected from aryl, R_5 , or R_6 ;

wherein W is (B):



25 wherein B^0 is $-O-$, $-S-$, or $-N(R_{B-0})-$;

B^1 and B^2 are independently selected from $=N-$, or $=C(R_{B-1})-$;

B^3 is $=N-$, or $=CH-$, provided that when both B^1 and B^2 are $=C(R_{B-1})-$ and B^3 is $=CH-$, only one $=C(R_{B-1})-$ can be $=CH-$, and further provided that when B^0 is $-O-$, B^2 is $=C(R_{B-1})-$ and B^3 is $=C(H)-$, B^1 cannot be $=N-$,

R_{B-0} is H, alkyl, cycloalkyl, heterocycloalkyl, haloalkyl, halocycloalkyl, haloheterocycloalkyl, substituted alkyl, limited substituted alkyl, substituted cycloalkyl, substituted heterocycloalkyl, or aryl, and provided that when B is (B-2) and B^3 is =N- and B^0 is N(R_{B-0}), R_{B-0} cannot be phenyl or substituted phenyl;

5 R_{B-1} is H, alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, haloalkyl, haloalkenyl, haloalkynyl, halocycloalkyl, haloheterocycloalkyl, substituted alkyl, substituted alkenyl, substituted alkynyl, substituted cycloalkyl, substituted heterocycloalkyl, limited substituted alkyl, limited substituted alkenyl, limited substituted alkynyl, aryl, -OR_{B-2}, -OR_{B-3}, -SR_{B-2}, -SR_{B-3}, F, Cl, Br, I, -N(R_{B-2})₂,
10 -N(R_{B-3})₂, -C(O)R_{B-2}, -C(O)R_{B-3}, -C(O)N(R_{B-2})₂, -C(O)N(R_{B-3})₂, -CN, -NR_{B-2}C(O)R_{B-4}, -S(O)₂N(R_{B-2})₂, -OS(O)₂R_{B-4}, -S(O)₂R_{B-2}, -S(O)₂R_{B-3}, -NR_{B-2}S(O)₂R_{B-2}, -N(H)C(O)N(H)R_{B-2}, -NO₂, R₅, and R₆;

Each R_{B-2} is independently H, alkyl, haloalkyl, substituted alkyl, cycloalkyl, halocycloalkyl, substituted cycloalkyl, heterocycloalkyl, haloheterocycloalkyl,
15 substituted heterocycloalkyl, R₅, R₆, phenyl, or substituted phenyl;

Each R_{B-3} is independently H, alkyl, haloalkyl, limited substituted alkyl, cycloalkyl, halocycloalkyl, substituted cycloalkyl, heterocycloalkyl, haloheterocycloalkyl, substituted heterocycloalkyl;

R_{B-4} is independently H, alkyl, cycloalkyl, heterocycloalkyl, haloalkyl,
20 halocycloalkyl, or haloheterocycloalkyl;

wherein W is (C):

(C) is a six-membered heterocyclic ring system having 1-2 nitrogen atoms or a 10-membered bicyclic-six-six-fused-ring system having up to two nitrogen atoms
25 within either or both rings, provided that no nitrogen is at a bridge of the bicyclic-six-six-fused-ring system, and further having 1-2 substituents independently selected from R_{C-1};

Each R_{C-1} is independently H, F, Cl, Br, I, alkyl, haloalkyl, substituted alkyl, alkenyl, haloalkenyl, substituted alkenyl, alkynyl, haloalkynyl, substituted alkynyl,
30 cycloalkyl, halocycloalkyl, substituted cycloalkyl, heterocycloalkyl, haloheterocycloalkyl, substituted heterocycloalkyl, lactam heterocycloalkyl, phenyl, substituted phenyl, -NO₂, -CN, -OR_{C-2}, -SR_{C-2}, -SOR_{C-2}, -SO₂R_{C-2}, -NR_{C-2}C(O)R_{C-3}, -NR_{C-2}C(O)R_{C-2}, -NR_{C-2}C(O)R_{C-4}, -N(R_{C-2})₂, -C(O)R_{C-2}, -C(O)₂R_{C-2}, -C(O)N(R_{C-2})₂,

-SCN, -NR_{C-2}C(O)R_{C-2}, -S(O)N(R_{C-2})₂, -S(O)₂N(R_{C-2})₂, -NR_{C-2}S(O)₂R_{C-2}, R₅, or R₆;

Each R_{C-2} is independently H, alkyl, cycloalkyl, heterocycloalkyl, alkyl substituted with 1 substituent selected from R_{C-5}, cycloalkyl substituted with 1 substituent selected from R_{C-5}, heterocycloalkyl substituted with 1 substituent selected from R_{C-5}, haloalkyl, halocycloalkyl, haloheterocycloalkyl, phenyl, or substituted phenyl;

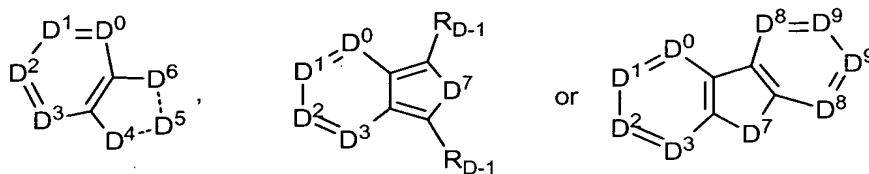
Each R_{C-3} is independently H, alkyl, or substituted alkyl;

R_{C-4} is H, alkyl, an amino protecting group, or an alkyl group having 1-3 substituents selected from F, Cl, Br, I, -OH, -CN, -NH₂, -NH(alkyl), or -N(alkyl)₂;

R_{C-5} is -CN, -CF₃, -NO₂, -OR_{C-6}, -SR_{C-6}, -N(R_{C-6})₂, -C(O)R_{C-6}, -SOR_{C-6}, -SO₂RR_{C-6}, -C(O)N(R_{C-6})₂, -NR_{C-6}C(O)R_{C-6}, -S(O)₂N(R_{C-6})₂, or -NR_{C-6}S(O)₂R_{C-6};

Each R_{C-6} is independently H, alkyl, cycloalkyl, heterocycloalkyl, haloalkyl, halocycloalkyl, or haloheterocycloalkyl;

wherein W is (D):



provided that the bond between the -C(=X)- group and the W group may be attached at any available carbon atom within the D group as provided in R_{D-1}, R_{D-3}, and R_{D-4};

D⁰, D¹, D², and D³ are N or C(R_{D-1}) provided that up to one of D⁰, D¹, D², or D³ is N and the others are C(R_{D-1}), further provided that when the core molecule is attached at D² and D⁰ or D¹ is N, D³ is C(H), and further provided that there is only one attachment to the core molecule;

D⁴---D⁵---D⁶ is selected from N(R_{D-2})-C(R_{D-3})=C(R_{D-3}), N=C(R_{D-3})-C(R_{D-4})₂, C(R_{D-3})=C(R_{D-3})-N(R_{D-2}), C(R_{D-3})₂-N(R_{D-2})-C(R_{D-3})₂, C(R_{D-4})₂-C(R_{D-3})=N, N(R_{D-2})-C(R_{D-3})₂-C(R_{D-3})₂, C(R_{D-3})₂-C(R_{D-3})₂-N(R_{D-2}), O-C(R_{D-3})=C(R_{D-3}), O-C(R_{D-3})₂-C(R_{D-3})₂, C(R_{D-3})₂-O-C(R_{D-3})₂, C(R_{D-3})=C(R_{D-3})-O, C(R_{D-3})₂-C(R_{D-3})₂-O, S-C(R_{D-3})=C(R_{D-3}), S-C(R_{D-3})₂-C(R_{D-3})₂, C(R_{D-3})₂-S-C(R_{D-3})₂, C(R_{D-3})=C(R_{D-3})-S, or C(R_{D-3})₂-C(R_{D-3})₂-S;

provided that when C(X) is attached to W at D² and D⁶ is O, N(R_{D-2}), or S, D⁴---D⁵ is not CH=CH;

and further provided that when C(X) is attached to W at D² and D⁴ is O, N(R_{D-2}), or S, D⁵---D⁶ is not CH=CH;

Each R_{D-1} is independently H, F, Br, I, Cl, -CN, -CF₃, -OR_{D-5}, -SR_{D-5}, -N(R_{D-5})₂, or a bond to -C(X)- provided that only one of R_{D-1}, R_{D-3}, and R_{D-4} is said
5 bond;

Each R_{D-2} is independently H, alkyl, haloalkyl, substituted alkyl, cycloalkyl, halocycloalkyl, substituted cycloalkyl, heterocycloalkyl, haloheterocycloalkyl, substituted heterocycloalkyl, R₅, or R₆;

Each R_{D-3} is independently H, F, Br, Cl, I, alkyl, substituted alkyl, haloalkyl, alkenyl, substituted alkenyl, haloalkenyl, alkynyl, substituted alkynyl, haloalkynyl, heterocycloalkyl, substituted heterocycloalkyl, lactam heterocycloalkyl, -CN, -NO₂, -OR_{D-10}, -C(O)N(R_{D-11})₂, -NR_{D-10}COR_{D-12}, -N(R_{D-10})₂, -SR_{D-10}, -S(O)₂R_{D-10}, -C(O)R_{D-12}, -CO₂R_{D-10}, aryl, R₅, R₆, a bond to -C(X)- provided that only one of R_{D-1}, R_{D-3}, and R_{D-4} is said bond;
10

Each R_{D-4} is independently H, F, Br, Cl, I, alkyl, substituted alkyl, haloalkyl, alkenyl, substituted alkenyl, haloalkenyl, alkynyl, substituted alkynyl, haloalkynyl, heterocycloalkyl, substituted heterocycloalkyl, lactam heterocycloalkyl, -CN, -NO₂, -OR_{D-10}, -C(O)N(R_{D-11})₂, -NR_{D-10}COR_{D-12}, -N(R_{D-11})₂, -SR_{D-10}, -CO₂R_{D-10}, aryl, R₅, R₆, a bond to -C(X)- provided that only one of R_{D-1}, R_{D-3}, and R_{D-4} is said bond;
15

Each R_{D-5} is independently H, C₁₋₃ alkyl, or C₂₋₄ alkenyl;
20

D⁷ is O, S, or N(R_{D-2});

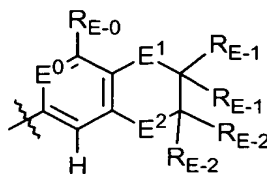
D⁸ and D⁹ are C(R_{D-1}), provided that when the molecule is attached to the phenyl moiety at D⁹, D⁸ is CH;

Each R_{D-10} is H, alkyl, cycloalkyl, haloalkyl, substituted phenyl, or substituted naphthyl;
25

Each R_{D-11} is independently H, alkyl, cycloalkyl, heterocycloalkyl, alkyl substituted with 1 substituent selected from R₁₃, cycloalkyl substituted with 1 substituent selected from R₁₃, heterocycloalkyl substituted with 1 substituent selected from R₁₃, haloalkyl, halocycloalkyl, haloheterocycloalkyl, phenyl, or substituted phenyl;
30

R_{D-12} is H, alkyl, substituted alkyl, cycloalkyl, haloalkyl, heterocycloalkyl, substituted heterocycloalkyl, substituted phenyl, or substituted naphthyl;

wherein W is (E):


$$E^0 \text{ is CH or N;}$$

R_{E-0} is H, F, Cl, Br, I, alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, haloalkyl, haloalkenyl, haloalkynyl, halocycloalkyl, haloheterocycloalkyl, substituted alkyl, substituted alkenyl, substituted alkynyl, substituted cycloalkyl, substituted heterocycloalkyl, aryl, R₅, R₆, -OR_{E-3}, -OR_{E-4}, -SR_{E-3}, -SR_{E-5}, -N(R_{E-3})₂, -NR_{E-3}R_{E-6}, -N(R_{E-6})₂, -C(O)R_{E-3}, -CN, -C(O)N(R_{E-3})₂, -NR_{E-3}C(O)R_{E-3}, -S(O)R_{E-3}, -S(O)R_{E-5}, -OS(O)₂R_{E-3}, -NR_{E-3}S(O)₂R_{E-3}, -NO₂, or -N(H)C(O)N(H)R_{E-3};

10 E¹ is O, CR_{E-1-1}, or C(R_{E-1-1})₂, provided that when E¹ is CR_{E-1-1}, one R_{E-1} is a bond to CR_{E-1-1}, and further provided that at least one of E¹ or E² is O;

Each R_{E-1-1} is independently H, F, Br, Cl, CN, alkyl, haloalkyl, substituted alkyl, alkynyl, cycloalkyl, -OR_E, or -N(R_E)₂, provided that at least one R_{E-1-1} is H when E¹ is C(R_{E-1-1})₂;

15 Each R_{E-1} is independently H, alkyl, substituted alkyl, haloalkyl, cycloalkyl, heterocycloalkyl, or a bond to E¹ provided that E¹ is CR_{E-1-1};

E^2 is O, $CR_{E-2,2}$, or $C(R_{E-2,2})_2$, provided that when E^2 is $CR_{E-2,2}$, one R_{E-2} is a bond to $CR_{E-2,2}$, and further provided that at least one of E^1 or E^2 is O;

Each R_{E-2-2} is independently H, F, Br, Cl, CN, alkyl, haloalkyl, substituted
20 alkyl, alkynyl, cycloalkyl, -OR_E, or -N(R_E)₂, provided that at least one R_{E-2-2} is H
when E² is C(R_{E-2-2})₂;

Each R_{E-2} is independently H, alkyl, substituted alkyl, haloalkyl, cycloalkyl, heterocycloalkyl, or a bond to E² provided that E² is CR_{E-2-2};

Each R_E is independently H, alkyl, cycloalkyl, heterocycloalkyl, haloalkyl,
25 halocycloalkyl, or haloheterocycloalkyl;

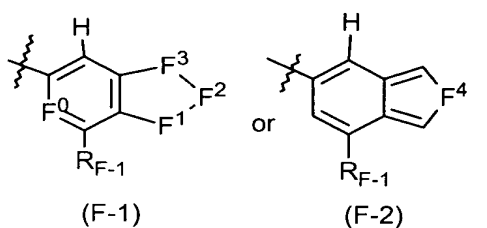
Each R_{E-3} is independently H, alkyl, haloalkyl, substituted alkyl, cycloalkyl, halocycloalkyl, substituted cycloalkyl, heterocycloalkyl, haloheterocycloalkyl, substituted heterocycloalkyl, R₅, R₆, phenyl, or phenyl having 1 substituent selected from R₉ and further having 0-3 substituents independently selected from F, Cl, Br, or I or substituted phenyl;

R_{E-4} is H, haloalkyl, substituted alkyl, cycloalkyl, halocycloalkyl, substituted cycloalkyl, heterocycloalkyl, haloheterocycloalkyl, substituted heterocycloalkyl, R_5 , R_6 , phenyl, or substituted phenyl;

Each R_{E-5} is independently H, haloalkyl, substituted alkyl, cycloalkyl,
 5 halocycloalkyl, substituted cycloalkyl, heterocycloalkyl, haloheterocycloalkyl, substituted heterocycloalkyl, R_5 , or R_6 ;

Each R_{E-6} is independently alkyl, haloalkyl, substituted alkyl, cycloalkyl, halocycloalkyl, substituted cycloalkyl, heterocycloalkyl, haloheterocycloalkyl, substituted heterocycloalkyl, R_5 , R_6 , phenyl, or phenyl having 1 substituent selected
 10 from R_9 and further having 0-3 substituents independently selected from F, Cl, Br, or I;

wherein W is (F):



15 F^0 is C(H) wherein $F^1 \text{---} F^2 \text{---} F^3$ is selected from O-C(R_{F-2})=N, O-C(R_{F-3})(R_{F-2})-N(R_{F-4}), O-C(R_{F-3})(R_{F-2})-S, O-N=C(R_{F-3}), O-C(R_{F-2})(R_{F-3})-O, S-C(R_{F-2})=N, S-C(R_{F-3})(R_{F-2})-N(R_{F-4}), S-N=C(R_{F-3}), N=C(R_{F-2})-O, N=C(R_{F-2})-S, N=C(R_{F-2})-N(R_{F-4}), N(R_{F-4})-N=C(R_{F-3}), N(R_{F-4})-C(R_{F-3})(R_{F-2})-O, N(R_{F-4})-C(R_{F-3})(R_{F-2})-S, N(R_{F-4})-C(R_{F-3})(R_{F-2})-N(R_{F-4}), C(R_{F-3})₂-O-N(R_{F-4}),
 20 C(R_{F-3})₂-N(R_{F-4})-O, C(R_{F-3})₂-N(R_{F-4})-S, C(R_{F-3})=N-O, C(R_{F-3})=N-S, C(R_{F-3})=N-N(R_{F-4}), or C(R_{F-3})₂-C(R_{F-2})(R_{F-3})-C(R_{F-3})₂;

F^0 is N wherein $F^1 \text{---} F^2 \text{---} F^3$ is selected from O-C(R_{F-2})=N, O-C(R_{F-3})(R_{F-2})-N(R_{F-4}), O-C(R_{F-3})(R_{F-2})-S, O-N=C(R_{F-3}), O-C(R_{F-2})(R_{F-3})-O, S-C(R_{F-2})=N, S-C(R_{F-3})(R_{F-2})-N(R_{F-4}), S-N=C(R_{F-3}), N=C(R_{F-2})-O, N=C(R_{F-2})-S,
 25 N=C(R_{F-2})-N(R_{F-4}), N(R_{F-4})-N=C(R_{F-3}), N(R_{F-4})-C(R_{F-3})(R_{F-2})-O, N(R_{F-4})-C(R_{F-3})(R_{F-2})-S, N(R_{F-4})-C(R_{F-3})(R_{F-2})-N(R_{F-4}), C(R_{F-3})₂-O-N(R_{F-4}), C(R_{F-3})₂-N(R_{F-4})-O, C(R_{F-3})₂-N(R_{F-4})-S, C(R_{F-3})=N-O, C(R_{F-3})=N-S, C(R_{F-3})=N-N(R_{F-4}), C(R_{F-3})=C(R_{F-2})-C(R_{F-3})₂, or C(R_{F-3})₂-C(R_{F-2})(R_{F-3})-C(R_{F-3})₂;

F^4 is N(R_{F-7}), O, or S;

30 R_{F-1} is H, F, Cl, Br, I, -CN, -CF₃, -OR_{F-8}, -SR_{F-8}, or -N(R_{F-8})₂;

R_{F-2} is H, F, alkyl, haloalkyl, substituted alkyl, lactam heterocycloalkyl, phenoxy, substituted phenoxy, R_5 , R_6 , $-N(R_{F-4})$ -aryl, $-N(R_{F-4})$ -substituted phenyl, $-N(R_{F-4})$ -substituted naphthyl, $-O$ -substituted phenyl, $-O$ -substituted naphthyl, $-S$ -substituted phenyl, $-S$ -substituted naphthyl, or alkyl substituted on the ω carbon with R_{F-9} ;

R_{F-3} is H, F, Br, Cl, I, alkyl, substituted alkyl, haloalkyl, alkenyl, substituted alkenyl, haloalkenyl, alkynyl, substituted alkynyl, haloalkynyl, heterocycloalkyl, substituted heterocycloalkyl, lactam heterocycloalkyl, $-CN$, $-NO_2$, $-OR_{F-8}$, $-C(O)N(R_{F-8})_2$, $-NHR_{F-8}$, $-NR_{F-8}COR_{F-8}$, $-N(R_{F-8})_2$, $-SR_{F-8}$, $-C(O)R_{F-8}$, $-CO_2R_{F-8}$, aryl, R_5 , or R_6 ;

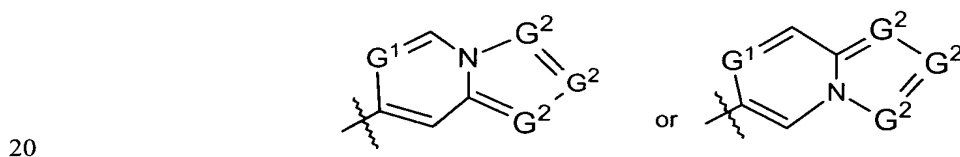
R_{F-4} is H, or alkyl;

R_{F-7} is H, alkyl, haloalkyl, substituted alkyl, cycloalkyl, halocycloalkyl, substituted cycloalkyl, phenyl, or phenyl having 1 substituent selected from R_9 and further having 0-3 substituents independently selected from F, Cl, Br, or I;

R_{F-8} is H, alkyl, substituted alkyl, cycloalkyl, haloalkyl, heterocycloalkyl, substituted heterocycloalkyl, substituted phenyl, or substituted naphthyl;

R_{F-9} is aryl, R_5 , or R_6 ;

wherein W is (G):



G^1 is N or CH;

Each G^2 is N or $C(R_{G-1})$, provided that no more than one G^2 N;

Each R_{G-1} is independently H, alkyl, substituted alkyl, haloalkyl, alkenyl, substituted alkenyl, haloalkenyl, alkynyl, substituted alkynyl, haloalkynyl, $-CN$, $-NO_2$, F, Br, Cl, I, $-C(O)N(R_{G-3})_2$, $-N(R_{G-3})_2$, $-SR_{G-6}$, $-S(O)_2R_{G-6}$, $-OR_{G-6}$, $-C(O)R_{G-6}$, $-CO_2R_{G-6}$, aryl, R_5 , R_6 , or two R_{G-1} on adjacent carbon atoms may combine for W to be a 6-5-6 fused-tricyclic-heteroaromatic-ring system optionally substituted on the newly formed ring where valency allows with 1-2 substituents independently selected from F, Cl, Br, I, and R_{G-2} ;

R_{G-2} is alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, haloalkyl, haloalkenyl, haloalkynyl, halocycloalkyl, haloheterocycloalkyl, $-OR_{G-8}$, $-SR_{G-8}$,

-S(O)₂R_{G-8}, -S(O)R_{G-8}, -OS(O)₂R_{G-8}, -N(R_{G-8})₂, -C(O)R_{G-8}, -C(S)R_{G-8}, -C(O)OR_{G-8},
 -CN, -C(O)N(R_{G-8})₂, -NR_{G-8}C(O)R_{G-8}, -S(O)₂N(R_{G-8})₂, -NR_{G-8}S(O)₂R_{G-8}, -NO₂,
 -N(R_{G-8})C(O)N(R_{G-8})₂, substituted alkyl, substituted alkenyl, substituted alkynyl,
 substituted cycloalkyl, substituted heterocycloalkyl, lactam heterocycloalkyl, phenyl,
 5 phenyl having 0-4 substituents independently selected from F, Cl, Br, I and R_{G-7},
 naphthyl, or naphthyl having 0-4 substituents independently selected from F, Cl, Br, I,
 or R_{G-7};

provided that when G² adjacent to the bridge N is C(R_{G-1}) and the other G² are
 CH, that R_{G-1} is other than H, F, Cl, I, alkyl, substituted alkyl or alkynyl;

10 Each R_{G-3} is independently H, alkyl, cycloalkyl, heterocycloalkyl, alkyl
 substituted with 1 substituent selected from R_{G-4}, cycloalkyl substituted with 1
 substituent selected from R_{G-4}, heterocycloalkyl substituted with 1 substituent selected
 from R_{G-4}, haloalkyl, halocycloalkyl, haloheterocycloalkyl, phenyl, or substituted
 phenyl;

15 R_{G-4} is -OR_{G-5}, -SR_{G-5}, -N(R_{G-5})₂, -C(O)R_{G-5}, -SOR_{G-5}, -SO₂R_{G-5},
 -C(O)N(R_{G-5})₂, -CN, -CF₃, -NR_{G-5}C(O)R_{G-5}, -S(O)₂N(R_{G-5})₂, -NR_{G-5}S(O)₂R_{G-5}, or
 -NO₂;

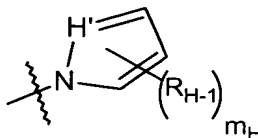
Each R_{G-5} is independently H, alkyl, cycloalkyl, heterocycloalkyl, haloalkyl,
 halocycloalkyl, or haloheterocycloalkyl;

20 R_{G-6} is H, alkyl, haloalkyl, substituted alkyl, cycloalkyl, halocycloalkyl,
 substituted cycloalkyl, phenyl, or phenyl having 0-4 substituents independently
 selected from F, Cl, Br, I, and R_{G-7};

R_{G-7} is alkyl, substituted alkyl, haloalkyl, -OR_{G-5}, -CN, -NO₂, -N(R_{G-3})₂;

Each R_{G-8} is independently H, alkyl, haloalkyl, substituted alkyl, cycloalkyl,
 25 halocycloalkyl, substituted cycloalkyl, heterocycloalkyl, haloheterocycloalkyl,
 substituted heterocycloalkyl, phenyl, or phenyl substituted with 0-4 independently
 selected from F, Cl, Br, I, or R_{G-7};

wherein W is (H)



30

H' is N or CH;

Each R_{H-1} is independently F, Cl, Br, I, -CN, -NO₂, alkyl, haloalkyl, substituted alkyl, alkenyl, haloalkenyl, substituted alkenyl, alkynyl, haloalkynyl, substituted alkynyl, cycloalkyl, halocycloalkyl, substituted cycloalkyl, heterocycloalkyl, haloheterocycloalkyl, substituted heterocycloalkyl, lactam heterocycloalkyl, aryl, R₅, R₆, -OR₈, -SR₈, -SOR₈, -SO₂R₈, -SCN, -S(O)N(R₈)₂, -S(O)₂N(R₈)₂, -C(O)R₈, -C(O)₂R₈, -C(O)N(R₈)₂, C(R₈)=N-OR₈, -NC(O)R₅, -NC(O)R_{H-3}, -NC(O)R₆, -N(R₈)₂, -NR₈C(O)R₈, -NR₈S(O)₂R₈, or two R_{H-1} on adjacent carbon atoms may fuse to form a 6-membered ring to give a 5-6 fused, bicyclic moiety where the 6-membered ring is optionally substituted with 1-3 substituents selected from R_{H-2} ;

m_H is 0, 1, or 2;

R_{H-2} is alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, haloalkyl, haloalkenyl, haloalkynyl, halocycloalkyl, haloheterocycloalkyl, -OR_{H-3}, -SR_{H-3}, -S(O)₂R_{H-3}, -S(O)R_{H-3}, -OS(O)₂R_{H-3}, -N(R_{H-3})₂, -C(O)R_{H-3}, -C(S)R_{H-3}, -C(O)OR_{H-3}, -CN, -C(O)N(R_{H-3})₂, -NR_{H-3}C(O)R_{H-3}, -S(O)₂N(R_{H-3})₂, -NR_{H-3}S(O)₂R_{H-3}, -NO₂, -N(R_{H-3})C(O)N(R_{H-3})₂, substituted alkyl, substituted alkenyl, substituted alkynyl, substituted cycloalkyl, substituted heterocycloalkyl, lactam heterocycloalkyl, phenyl, phenyl having 0-4 substituents independently selected from F, Cl, Br, I and R₇, naphthyl, naphthyl having 0-4 substituents independently selected from F, Cl, Br, I, or R₇, or two R_{H-2} on adjacent carbon atoms may combine to form a three-ring-fused-5-6-6 system optionally substituted with up to 3 substituents independently selected from Br, Cl, F, I, -CN, -NO₂, -CF₃, -N(R_{H-3})₂, -N(R_{H-3})C(O)R_{H-3}, alkyl, alkenyl, and alkynyl;

Each R_{H-3} is independently H, alkyl, haloalkyl, substituted alkyl, cycloalkyl, halocycloalkyl, substituted cycloalkyl, heterocycloalkyl, haloheterocycloalkyl, substituted heterocycloalkyl, phenyl, or phenyl substituted with 0-4 independently selected from F, Cl, Br, I, or R₇;

or pharmaceutical composition, pharmaceutically acceptable salt, racemic mixture, or pure enantiomer thereof.

6. The method of claim 5, wherein the Acetylcholinesterase inhibitor is physostigmine, aricept, rivastigmine, galantamine, monoamine acridines and derivatives, piperidinyl-alkanoyl heterocyclic compounds, N-benzyl-piperidine

derivatives, 4-(1-benzylpiperidyl)-substituted fused quinoline derivatives, and cyclic amide derivatives.

7. The method of claim 5, wherein X is O, R₁ is H, R₂ is absent, R_{2,3} is H, each
 5 R₃ is H, R₄ is H and W is 4-chlorobenz-1-yl; dibenzo[b,d]thiophene-2-yl;
 isoquinoline-3-yl; furo[2,3-c]pyridine-5-yl; 1,3-benzodioxole-5-yl; 2,3-dihydro-1,4-
 benzodioxine-6-yl; 1,3-benzoxazole-5-yl; thieno[2,3-c]pyridine-5-yl; thieno[3,2-
 c]pyridine-6-yl; [1]benzothieno[3,2-c]pyridine-3-yl; 1,3-benzothiazole-6-yl;
 thieno[3,4-c]pyridine-6-yl; 2,3-dihydro-1-benzofuran-5-yl; 1-benzofuran-5-yl;
 10 furo[3,2-c]pyridine-6-yl; [1]benzothieno[2,3-c]pyridine-3-yl; dibenzo[b,d]furan-2-yl;
 1-benzofuran-6-yl; 2-naphthyl; 1H-indole-6-yl; pyrrolo[1,2-c]pyrimidine-3-yl; 1-
 benzothiophene-5-yl; 1-benzothiophene-5-yl; 1-benzothiophene-6-yl; pyrrolo[1,2-
 a]pyrazine-3-yl; 1H-indole-6-yl; pyrazino[1,2-a]indole-3-yl; 1,3-benzothiazole-6-yl;
 [1]benzofuro[2,3-c]pyridine-3-yl; [1]benzofuro[2,3-c]pyridine-3-yl; 2H-chromene-6-
 15 yl; indolizine-6-yl; and [1,3]dioxolo[4,5-c]pyridine-6-yl; any of which is optionally
 substituted as allowed in claim 5.

8. The method of claim 7, wherein the agonist is
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-4-chlorobenzamide;
 20 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]dibenzo[b,d]thiophene-2-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]isoquinoline-3-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]furo[2,3-c]pyridine-5-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-1,3-benzodioxole-5-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-2-methylfuro[2,3-c]pyridine-5-carboxamide;
 25 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-2,3-dihydro-1,4-benzodioxine-6-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-3-methylfuro[2,3-c]pyridine-5-carboxamide;
 N-[(1S,2R,4R)-7-azabicyclo[2.2.1]hept-2-yl]isoquinoline-3-carboxamide;
 N-[(1S,2R,4R)-7-azabicyclo[2.2.1]hept-2-yl]-3-methylfuro[2,3-c]pyridine-5-
 carboxamide;
 30 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-1,3-benzoxazole-5-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-2-methyl-1,3-benzoxazole-5-carboxamide;
 N-[(1S,2R,4R)-7-azabicyclo[2.2.1]hept-2-yl]thieno[2,3-c]pyridine-5-carboxamide;
 N-[(1S,2R,4R)-7-azabicyclo[2.2.1]hept-2-yl]thieno[3,2-c]pyridine-6-carboxamide;

- N-[(1S,2R,4R)-7-azabicyclo[2.2.1]hept-2-yl]furo[2,3-c]pyridine-5-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-3-ethylfuro[2,3-c]pyridine-5-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-3-isopropylfuro[2,3-c]pyridine-5-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]thieno[2,3-c]pyridine-5-carboxamide;
 5 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]thieno[3,2-c]pyridine-6-carboxamide;
 5-{[(2R)-7-azoniabicyclo[2.2.1]hept-2-ylamino]carbonyl}-3-ethylfuro[2,3-c]pyridin-6-ium dichloride;
 5-{[(2R)-7-azoniabicyclo[2.2.1]hept-2-ylamino]carbonyl}-3-isopropylfuro[2,3-c]pyridin-6-ium dichloride;
 10 N-[(3R,4S)-1-azabicyclo[2.2.1]hept-3-yl]furo[2,3-c]pyridine-5-carboxamide;
 N-1-azabicyclo[2.2.2]oct-3-yl[1]benzothieno[3,2-c]pyridine-3-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-1,3-benzothiazole-6-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-3-chlorofuro[2,3-c]pyridine-5-carboxamide;
 N-1-azabicyclo[2.2.2]oct-3-ylfuro[2,3-c]pyridine-5-carboxamide;
 15 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]thieno[3,4-c]pyridine-6-carboxamide;
 N-[(3R,5R)-1-azabicyclo[3.2.1]oct-3-yl]-3-methylfuro[2,3-c]pyridine-5-carboxamide;
 N-[(3R,4S)-1-azabicyclo[2.2.1]hept-3-yl]-3-methylfuro[2,3-c]pyridine-5-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-2,3-dihydro-1-benzofuran-5-carboxamide;
 20 N-[(3R,4S)-1-azabicyclo[2.2.1]hept-3-yl]thieno[2,3-c]pyridine-5-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-1-benzofuran-5-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]furo[3,2-c]pyridine-6-carboxamide;
 N-[(3R,4S)-1-azabicyclo[2.2.1]hept-3-yl]thieno[3,2-c]pyridine-6-carboxamide;
 N-[(3R,4S)-1-azabicyclo[2.2.1]hept-3-yl]3-ethylfuro[2,3-c]pyridine-5-carboxamide;
 25 N-[(3R,4S)-1-azabicyclo[2.2.1]hept-3-yl]3-isopropylfuro[2,3-c]pyridine-5-carboxamide;
 N-[(1S,2R,4R)-7-azabicyclo[2.2.1]hept-2-yl]-3-chlorofuro[2,3-c]pyridine-5-carboxamide;
 N-[(3R,4S)-1-azabicyclo[2.2.1]hept-3-yl]3-chlorofuro[2,3-c]pyridine-5-carboxamide;
 30 N-[(2S,3R)-2-methyl-1-azabicyclo[2.2.2]oct-3-yl]furo[2,3-c]pyridine-5-carboxamide;
 N-[(3R,5R)-1-azabicyclo[3.2.1]oct-3-yl]-4-chlorobenzamide;
 N-[(1S,2R,4R)-7-azabicyclo[2.2.1]hept-2-yl]thieno[3,4-c]pyridine-6-carboxamide;
 N-[(1S,2R,4R)-7-azabicyclo[2.2.1]hept-2-yl]dibenzo[b,d]thiophene-2-carboxamide;

- N-[(3R,4S)-1-azabicyclo[2.2.1]hept-3-yl]-1-benzofuran-5-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl][1]benzothieno[2,3-c]pyridine-3-carboxamide;
 N-[(1S,2R,4R)-7-azabicyclo[2.2.1]hept-2-yl][1]benzothieno[2,3-c]pyridine-3-carboxamide;
 5 N-[(1S,2R,4R)-7-azabicyclo[2.2.1]hept-2-yl]-1-benzofuran-5-carboxamide;
 N-[(1S,2R,4R)-7-azabicyclo[2.2.1]hept-2-yl]dibenzo[b,d]furan-2-carboxamide;
 N-[(3R,5R)-1-azabicyclo[3.2.1]oct-3-yl]furo[2,3-c]pyridine-5-carboxamide;
 N-[(3R,5R)-1-azabicyclo[3.2.1]oct-3-yl]furo[2,3-c]pyridine-5-carboxamide;
 N-[(3R,5R)-1-azabicyclo[3.2.1]oct-3-yl]-1-benzofuran-5-carboxamide;
 10 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-3-bromofuro[2,3-c]pyridine-5-carboxamide;
 N-[(1S,2R,4R)-7-azabicyclo[2.2.1]hept-2-yl]-3-bromofuro[2,3-c]pyridine-5-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-1-benzofuran-6-carboxamide;
 N-[(2S,3R)-2-methyl-1-azabicyclo[2.2.2]oct-3-yl]-2-naphthamide;
 15 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]pyrrolo[1,2-c]pyrimidine-3-carboxamide;
 N-[(3R,5R)-1-azabicyclo[3.2.1]oct-3-yl]thieno[2,3-c]pyridine-5-carboxamide;
 N-[(3R,5R)-1-azabicyclo[3.2.1]oct-3-yl]thieno[3,2-c]pyridine-6-carboxamide;
 N-[(2S,3R)-2-methyl-1-azabicyclo[2.2.2]oct-3-yl]furo[2,3-c]pyridine-5-carboxamide;
 N-[(3R,4S)-1-azabicyclo[2.2.1]hept-3-yl]-1H-indole-6-carboxamide;
 20 N-[(2S,3R)-2-methyl-1-azabicyclo[2.2.2]oct-3-yl]thieno[2,3-c]pyridine-5-carboxamide;
 3-methyl-N-[(2S,3R)-2-methyl-1-azabicyclo[2.2.2]oct-3-yl]furo[2,3-c]pyridine-5-carboxamide;
 N-[(2S,3R)-2-methyl-1-azabicyclo[2.2.2]oct-3-yl]-1-benzofuran-5-carboxamide;
 25 N-[(2S,3R)-2-methyl-1-azabicyclo[2.2.2]oct-3-yl]thieno[3,2-c]pyridine-6-carboxamide;
 N-[(2S,3R)-2-methyl-1-azabicyclo[2.2.2]oct-3-yl]pyrrolo[1,2-c]pyrimidine-3-carboxamide;
 N-[(2S,3R)-2-methyl-1-azabicyclo[2.2.2]oct-3-yl]-1,3-benzothiazole-6-carboxamide;
 30 N-[(3R,5R)-1-azabicyclo[3.2.1]oct-3-yl]pyrrolo[1,2-c]pyrimidine-3-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-1-benzothiophene-5-carboxamide;
 N-[(1S,2R,4R)-7-azabicyclo[2.2.1]hept-2-yl]pyrrolo[1,2-c]pyrimidine-3-carboxamide;
 N-[(3R,4S)-1-azabicyclo[2.2.1]hept-3-yl]pyrrolo[1,2-c]pyrimidine-3-carboxamide;

- N-[(3R,4S)-1-azabicyclo[2.2.1]hept-3-yl]-3-bromofuro[2,3-c]pyridine-5-carboxamide;
 N-[(3R,4S)-1-azabicyclo[2.2.1]hept-3-yl]-1,3-benzodioxole-5-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-3-bromo-1-benzofuran-5-carboxamide;
 N-[(1S,2R,4R)-7-azabicyclo[2.2.1]hept-2-yl]-3-bromo-1-benzofuran-5-carboxamide;
 5 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-3-bromothieno[2,3-c]pyridine-5-carboxamide;
 N-[(1S,2R,4R)-7-azabicyclo[2.2.1]hept-2-yl]-3-bromothieno[2,3-c]pyridine-5-carboxamide;
 N-[(3R,4S)-1-azabicyclo[2.2.1]hept-3-yl]-1-benzothiophene-5-carboxamide;
 N-[(3S)-1-azabicyclo[2.2.2]oct-3-yl]furo[2,3-c]pyridine-5-carboxamide;
 10 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-3-methyl-1-benzofuran-5-carboxamide;
 N-[(1S,2R,4R)-7-azabicyclo[2.2.1]hept-2-yl]-3-methyl-1-benzofuran-5-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-2-methyl-1-benzofuran-6-carboxamide;
 N-[(3R,5R)-1-azabicyclo[3.2.1]oct-3-yl]-1-benzofuran-6-carboxamide;
 N-[(2S,3R)-2-methyl-1-azabicyclo[2.2.2]oct-3-yl]-1-benzofuran-6-carboxamide;
 15 N-[(2S,3R)-2-methyl-1-azabicyclo[2.2.2]oct-3-yl]-1-benzothiophene-5-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-1-benzothiophene-6-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]pyrrolo[1,2-a]pyrazine-3-carboxamide;
 N-[(3R,4S)-1-azabicyclo[2.2.1]hept-3-yl]-1-benzothiophene-6-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-1-methyl-1H-indole-6-carboxamide;
 20 N-[(3S)-1-azabicyclo[2.2.2]oct-3-yl]-1-benzofuran-5-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-3-isopropyl-1-benzofuran-5-carboxamide;
 N-[(1S,2R,4R)-7-azabicyclo[2.2.1]hept-2-yl]-3-isopropyl-1-benzofuran-5-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-3-ethynylfuro[2,3-c]pyridine-5-carboxamide;
 25 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-1H-indazole-6-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-2-methyl-1-benzofuran-5-carboxamide;
 N-[(1S,2R,4R)-7-azabicyclo[2.2.1]hept-2-yl]-2-methyl-1-benzofuran-5-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]pyrazino[1,2-a]indole-3-carboxamide;
 3-bromo-N-[(2S,3R)-2-methyl-1-azabicyclo[2.2.2]oct-3-yl]furo[2,3-c]pyridine-5-carboxamide;
 30 N-[(3R,5R)-1-azabicyclo[3.2.1]oct-3-yl]pyrrolo[1,2-a]pyrazine-3-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-7-methoxy-2-naphthamide;
 N-[(1S,2R,4R)-7-azabicyclo[2.2.1]hept-2-yl]pyrrolo[1,2-a]pyrazine-3-carboxamide;

- N-[(3R,5R)-1-azabicyclo[3.2.1]oct-3-yl]-1,3-benzothiazole-6-carboxamide;
 N-[(3R,4S)-1-azabicyclo[2.2.1]hept-3-yl]-3-bromo-1-benzofuran-6-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl][1]benzofuro[2,3-c]pyridine-3-carboxamide;
 N-[(1S,2R,4R)-7-azabicyclo[2.2.1]hept-2-yl][1]benzofuro[2,3-c]pyridine-3-
 5 carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-3-ethynyl-1-benzofuran-5-carboxamide;
 N-[(1S,2R,4R)-7-azabicyclo[2.2.1]hept-2-yl]-3-ethynyl-1-benzofuran-5-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-2H-chromene-6-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-3-prop-1-ynyl-1-benzofuran-5-carboxamide;
 10 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-2-phenyl-1,3-benzodioxole-5-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-6-bromopyrrolo[1,2-a]pyrazine-3-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-3-prop-1-ynylfuro[2,3-c]pyridine-5-
 carboxamide;
 N-[(2S,3R)-2-methyl-1-azabicyclo[2.2.2]oct-3-yl]pyrrolo[1,2-a]pyrazine-3-
 15 carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]indolizine-6-carboxamide;
 2-amino-N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-1,3-benzothiazole-6-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-6-ethynylpyrrolo[1,2-a]pyrazine-3-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-8-methoxy-2-naphthamide;
 20 N-[(2S,3R)-2-methyl-1-azabicyclo[2.2.2]oct-3-yl]indolizine-6-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl][1,3]dioxolo[4,5-c]pyridine-6-carboxamide;
 N-[(1S,2R,4R)-7-azabicyclo[2.2.1]hept-2-yl][1,3]dioxolo[4,5-c]pyridine-6-
 carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-3-cyano-1-benzofuran-5-carboxamide;
 25 N-[(3R,4S)-1-azabicyclo[2.2.1]hept-3-yl][1,3]dioxolo[4,5-c]pyridine-6-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-3-ethyl-2,3-dihydro-1,4-benzodioxine-6-
 carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-7-hydroxy-2-naphthamide;
 N-[(1S,2R,4R)-7-azabicyclo[2.2.1]hept-2-yl]-3-ethynylfuro[2,3-c]pyridine-5-
 30 carboxamide;
 N-[(1S,2R,4R)-7-azabicyclo[2.2.1]hept-2-yl]-6-chloroisoquinoline-3-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-3-ethyl-2,3-dihydro-1,4-benzodioxine-6-
 carboxamide;

N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-3-ethyl-2,3-dihydro-1,4-benzodioxine-6-carboxamide;

N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-6-methylisoquinoline-3-carboxamide;

N-[(1S,2R,4R)-7-azabicyclo[2.2.1]hept-2-yl]-6-methylisoquinoline-3-carboxamide;

5 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-3-cyanofuro[2,3-c]pyridine-5-carboxamide;

N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-2-naphthamide; and

N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]dibenzo[b,d]furan-2-carboxamide, provided that the agonist is a free base or a pharmaceutically acceptable salt thereof.

10 9. The method of claim 8, wherein the disease or condition is cognitive and attention deficit symptoms of Alzheimer's, neurodegeneration associated with diseases such as Alzheimer's disease, pre-senile dementia (mild cognitive impairment), senile dementia, amyotrophic lateral sclerosis, traumatic brain injury, behavioral and cognitive problems in general and associated with brain tumors, AIDS
15 dementia complex, dementia associated with Down's syndrome, dementia associated with Lewy Bodies, Huntington's disease, Parkinson's disease, age-related macular degeneration.

10. The method of claim 8, wherein the Acetylcholinesterase inhibitor is
20 physostigmine, aricept, rivastigmine, galantamine, monoamine acridines and derivatives, piperidiny-alkanoyl heterocyclic compounds, N-benzyl-piperidine derivatives, 4-(1-benzylpiperidyl)-substituted fused quinoline derivatives, and cyclic amide derivatives.

25 11. The method of claim 10, wherein the disease or condition is cognitive and attention deficit symptoms of Alzheimer's, neurodegeneration associated with diseases such as Alzheimer's disease, pre-senile dementia (mild cognitive impairment), senile dementia, amyotrophic lateral sclerosis, traumatic brain injury, behavioral and cognitive problems in general and associated with brain tumors, AIDS
30 dementia complex, dementia associated with Down's syndrome, dementia associated with Lewy Bodies, Huntington's disease, Parkinson's disease, age-related macular degeneration.

12. The method of claim 1, wherein the agonist is administered with an effective amount of the beta secretase inhibitor and optionally with an effective amount of the acetylcholineesterase inhibitor and the gamma secretase inhibitor.

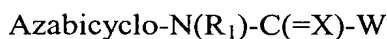
5 13. The method of claim 1, wherein the agonist is administered with an effective amount of the acetylcholineesterase inhibitor and optionally with an effective amount of the beta secretase inhibitor and the gamma secretase inhibitor.

10 14. The method of claim 13, wherein the acetylcholineesterase inhibitor is physostigmine, aricept, rivastigmine, galantamine, monoamine acridines and derivatives, piperidinyl-alkanoyl heterocyclic compounds, N-benzyl-piperidine derivatives, 4-(1-benzylpiperidyl)-substituted fused quinoline derivatives, and cyclic amide derivatives.

15 15. The method of claim 1, wherein the agonist is administered with an effective amount of the gamma secretase inhibitor and optionally with an effective amount of the beta secretase inhibitor and the acetylcholineesterase inhibitor.

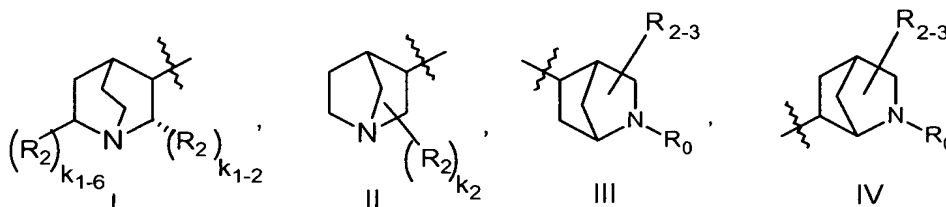
16. A composition comprising an effective amount of an alpha 7 nAChR full agonist and at least one of an effective amount of a beta secretase inhibitor, effective amount of an acetylcholineesterase inhibitor, and an effective amount of a gamma secretase inhibitor.

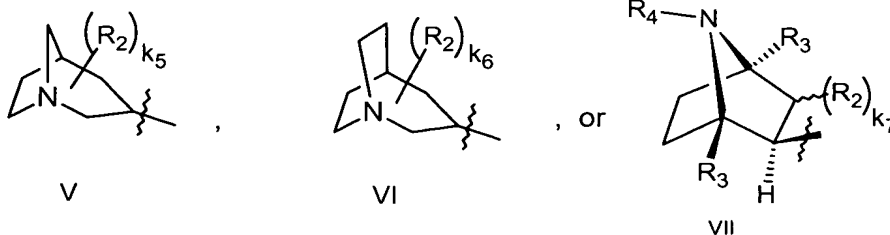
17. The composition of claim 16, wherein the alpha 7 nAChR full agonist is a compound of formula I:



Formula I

wherein Azabicyclo is





wherein X is O, or S;

R₀ is H, lower alkyl, substituted lower alkyl, or lower haloalkyl;

Each R₁ is H, alkyl, cycloalkyl, haloalkyl, substituted phenyl, or substituted
5 naphthyl;

Each R₂ is independently F, Cl, Br, I, alkyl, substituted alkyl, haloalkyl,
cycloalkyl, aryl, or R₂ is absent provided that k₁₋₂, k₁₋₆, k₂, k₅, k₆, or k₇ is 0;

k₁₋₂ is 0 or 1;

k₁₋₆ is 0 or 1, provided that the sum of k₁₋₂ and k₁₋₆ is one;

10 k₂ is 0 or 1;

k₅ is 0, 1, or 2;

k₆ is 0, 1, or 2;

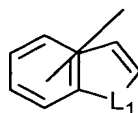
k₇ is 0 or 1;

R₂₋₃ is H, F, Cl, Br, I, alkyl, haloalkyl, substituted alkyl, cycloalkyl, or aryl;

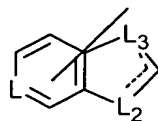
15 Each R₃ is independently H, alkyl, or substituted alkyl;

R₄ is H, alkyl, an amino protecting group, or an alkyl group having 1-3
substituents selected from F, Cl, Br, I, -OH, -CN, -NH₂, -NH(alkyl), or -N(alkyl)₂;

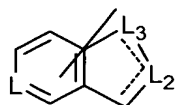
R₅ is 5-membered heteroaromatic mono-cyclic moieties containing within the
ring 1-3 heteroatoms independently selected from the group consisting of -O-, =N-,
20 -N(R₁₀)-, and -S-, and having 0-1 substituent selected from R₉ and further having 0-3
substituents independently selected from F, Cl, Br, or I, or R₅ is 9-membered fused-
ring moieties having a 6-membered ring fused to a 5-membered ring and having the
formula



25 wherein L₁ is O, S, or NR₁₀,



wherein L is CR₁₂ or N, L₂ and L₃ are independently selected from CR₁₂, C(R₁₂)₂, O, S, N, or NR₁₀, provided that both L₂ and L₃ are not simultaneously O, simultaneously S, or simultaneously O and S, or



5

wherein L is CR₁₂ or N, and L₂ and L₃ are independently selected from CR₁₂, O, S, N, or NR₁₀, and each 9-membered fused-ring moiety having 0-1 substituent selected from R₉ and further having 0-3 substituent(s) independently selected from F, Cl, Br, or I, wherein the R₅ moiety attaches to other substituents as defined in formula I at any

10 position as valency allows;

R₆ is 6-membered heteroaromatic mono-cyclic moieties containing within the ring 1-3 heteroatoms selected from =N- and having 0-1 substituent selected from R₉ and 0-3 substituent(s) independently selected from F, Cl, Br, or I, or R₆ is 10-membered heteroaromatic bi-cyclic moieties containing within one or both rings 1-3
15 heteroatoms selected from =N-, including, but not limited to, quinolinyl or isoquinolinyl, each 10-membered fused-ring moiety having 0-1 substituent selected from R₉ and 0-3 substituent(s) independently selected from F, Cl, Br, or I, wherein the R₆ moiety attaches to other substituents as defined in formula I at any position as valency allows;

20 R₇ is alkyl, substituted alkyl, haloalkyl, -OR₁₁, -CN, -NO₂, -N(R₈)₂;

Each R₈ is independently H, alkyl, cycloalkyl, heterocycloalkyl, alkyl substituted with 1 substituent selected from R₁₃, cycloalkyl substituted with 1 substituent selected from R₁₃, heterocycloalkyl substituted with 1 substituent selected from R₁₃, haloalkyl, halocycloalkyl, haloheterocycloalkyl, phenyl, or substituted
25 phenyl;

R₉ is alkyl, cycloalkyl, heterocycloalkyl, haloalkyl, halocycloalkyl, haloheterocycloalkyl, -OR₁₄, -SR₁₄, -N(R₁₄)₂, -C(O)R₁₄, -C(O)N(R₁₄)₂, -CN, -NR₁₄C(O)R₁₄, -S(O)₂N(R₁₄)₂, -NR₁₄S(O)₂R₁₄, -NO₂, alkyl substituted with 1-4 substituent(s) independently selected from F, Cl, Br, I, or R₁₃, cycloalkyl substituted
30 with 1-4 substituent(s) independently selected from F, Cl, Br, I, or R₁₃, or

heterocycloalkyl substituted with 1-4 substituent(s) independently selected from F, Cl, Br, I, or R_{13} ;

R_{10} is H, alkyl, haloalkyl, substituted alkyl, cycloalkyl, halocycloalkyl, substituted cycloalkyl, phenyl, or phenyl having 1 substituent selected from R_7 and
5 further having 0-3 substituents independently selected from F, Cl, Br, or I;

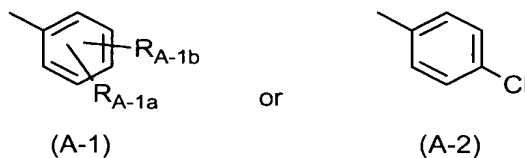
Each R_{11} is independently H, alkyl, cycloalkyl, heterocycloalkyl, haloalkyl, halocycloalkyl, or haloheterocycloalkyl;

Each R_{12} is independently H, F, Cl, Br, I, alkyl, cycloalkyl, heterocycloalkyl, haloalkyl, halocycloalkyl, haloheterocycloalkyl, substituted alkyl, substituted
10 cycloalkyl, substituted heterocycloalkyl, -CN, -NO₂, -OR₁₄, -SR₁₄, -N(R_{14})₂, -C(O) R_{14} , -C(O)N(R_{14})₂, -NR₁₄C(O) R_{14} , -S(O)₂N(R_{14})₂, -NR₁₄S(O)₂ R_{14} , or a bond directly or indirectly attached to the core molecule, provided that there is only one said bond to the core molecule within the 9-membered fused-ring moiety, further provided that where valency allows the fused-ring moiety has 0-1 substituent selected from
15 alkyl, cycloalkyl, heterocycloalkyl, haloalkyl, halocycloalkyl, haloheterocycloalkyl, substituted alkyl, substituted cycloalkyl, substituted heterocycloalkyl, -OR₁₄, -SR₁₄, -N(R_{14})₂, -C(O) R_{14} , -NO₂, -C(O)N(R_{14})₂, -CN, -NR₁₄C(O) R_{14} , -S(O)₂N(R_{14})₂, or -NR₁₄S(O)₂ R_{14} , and further provided that the fused-ring moiety has 0-3 substituent(s) selected from F, Cl, Br, or I;

20 R_{13} is -OR₁₄, -SR₁₄, -N(R_{14})₂, -C(O) R_{14} , -C(O)N(R_{14})₂, -CN, -CF₃, -NR₁₄C(O) R_{14} , -S(O)₂N(R_{14})₂, -NR₁₄S(O)₂ R_{14} , or -NO₂;

Each R_{14} is independently H, alkyl, cycloalkyl, heterocycloalkyl, haloalkyl, halocycloalkyl, or haloheterocycloalkyl;

25 wherein W is (A):



wherein R_{A-1a} is H, alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, haloalkyl, haloalkenyl, haloalkynyl, halocycloalkyl, haloheterocycloalkyl, substituted alkyl, substituted alkenyl, substituted alkynyl, substituted cycloalkyl, substituted
30 heterocycloalkyl, aryl, - R_5 , R_6 , -OR_{A-3}, -OR_{A-4}, -SR_{A-3}, F, Cl, Br, I, -N(R_{A-3})₂, -N(R_{A-5})₂, -C(O) R_{A-3} , -C(O) R_{A-5} , -CN, -C(O)N(R_{A-3})₂, -C(O)N(R_{A-6})₂,

$-\text{NR}_{\text{A-3}}\text{C}(\text{O})\text{R}_{\text{A-3}}$, $-\text{S}(\text{O})\text{R}_{\text{A-3}}$, $-\text{OS}(\text{O})_2\text{R}_{\text{A-3}}$, $-\text{NR}_{\text{A-3}}\text{S}(\text{O})_2\text{R}_{\text{A-3}}$, $-\text{NO}_2$, and $-\text{N}(\text{H})\text{C}(\text{O})\text{N}(\text{H})\text{R}_{\text{A-3}}$;

$\text{R}_{\text{A-1b}}$ is $-\text{O}-\text{R}_{\text{A-3}}$, $-\text{S}-\text{R}_{\text{A-3}}$, $-\text{S}(\text{O})-\text{R}_{\text{A-3}}$, $-\text{C}(\text{O})-\text{R}_{\text{A-7}}$, and alkyl substituted on the ω carbon with $\text{R}_{\text{A-7}}$;

5 Each $\text{R}_{\text{A-3}}$ is independently selected from H, alkyl, haloalkyl, substituted alkyl, cycloalkyl, halocycloalkyl, substituted cycloalkyl, heterocycloalkyl, haloheterocycloalkyl, substituted heterocycloalkyl, R_5 , R_6 , phenyl, or substituted phenyl;

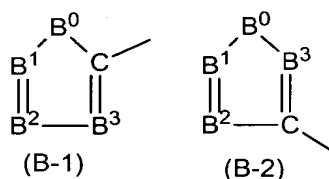
$\text{R}_{\text{A-4}}$ is selected from cycloalkyl, halocycloalkyl, substituted cycloalkyl, heterocycloalkyl, haloheterocycloalkyl, or substituted heterocycloalkyl;

10 Each $\text{R}_{\text{A-5}}$ is independently selected from cycloalkyl, halocycloalkyl, substituted cycloalkyl, heterocycloalkyl, haloheterocycloalkyl, substituted heterocycloalkyl, R_5 , R_6 , phenyl, or substituted phenyl;

Each $\text{R}_{\text{A-6}}$ is independently selected from alkyl, haloalkyl, substituted alkyl, cycloalkyl, halocycloalkyl, substituted cycloalkyl, heterocycloalkyl, haloheterocycloalkyl, substituted heterocycloalkyl, R_5 , R_6 , phenyl, or substituted phenyl;

$\text{R}_{\text{A-7}}$ is selected from aryl, R_5 , or R_6 ;

wherein W is (B):



20 wherein B^0 is $-\text{O}-$, $-\text{S}-$, or $-\text{N}(\text{R}_{\text{B-0}})-$;

B^1 and B^2 are independently selected from $=\text{N}-$, or $=\text{C}(\text{R}_{\text{B-1}})-$;

B^3 is $=\text{N}-$, or $=\text{CH}-$, provided that when both B^1 and B^2 are $=\text{C}(\text{R}_{\text{B-1}})-$ and B^3 is $=\text{CH}-$, only one $=\text{C}(\text{R}_{\text{B-1}})-$ can be $=\text{CH}-$, and further provided that when B^0 is $-\text{O}-$, B^2 is $=\text{C}(\text{R}_{\text{B-1}})-$ and B^3 is $=\text{C}(\text{H})-$, B^1 cannot be $=\text{N}-$,

25 $\text{R}_{\text{B-0}}$ is H, alkyl, cycloalkyl, heterocycloalkyl, haloalkyl, halocycloalkyl, haloheterocycloalkyl, substituted alkyl, limited substituted alkyl, substituted cycloalkyl, substituted heterocycloalkyl, or aryl, and provided that when B is (B-2) and B^3 is $=\text{N}-$ and B^0 is $\text{N}(\text{R}_{\text{B-0}})$, $\text{R}_{\text{B-0}}$ cannot be phenyl or substituted phenyl;

$\text{R}_{\text{B-1}}$ is H, alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, haloalkyl, haloalkenyl, haloalkynyl, halocycloalkyl, haloheterocycloalkyl, substituted alkyl,

substituted alkenyl, substituted alkynyl, substituted cycloalkyl, substituted heterocycloalkyl, limited substituted alkyl, limited substituted alkenyl, limited substituted alkynyl, aryl, -OR_{B-2}, -OR_{B-3}, -SR_{B-2}, -SR_{B-3}, F, Cl, Br, I, -N(R_{B-2})₂, -N(R_{B-3})₂, -C(O)R_{B-2}, -C(O)R_{B-3}, -C(O)N(R_{B-2})₂, -C(O)N(R_{B-3})₂, -CN,
 5 -NR_{B-2}C(O)R_{B-4}, -S(O)₂N(R_{B-2})₂, -OS(O)₂R_{B-4}, -S(O)₂R_{B-2}, -S(O)₂R_{B-3}, -NR_{B-2}S(O)₂R_{B-2}, -N(H)C(O)N(H)R_{B-2}, -NO₂, R₅, and R₆;

Each R_{B-2} is independently H, alkyl, haloalkyl, substituted alkyl, cycloalkyl, halocycloalkyl, substituted cycloalkyl, heterocycloalkyl, haloheterocycloalkyl, substituted heterocycloalkyl, R₅, R₆, phenyl, or substituted phenyl;

10 Each R_{B-3} is independently H, alkyl, haloalkyl, limited substituted alkyl, cycloalkyl, halocycloalkyl, substituted cycloalkyl, heterocycloalkyl, haloheterocycloalkyl, substituted heterocycloalkyl;

R_{B-4} is independently H, alkyl, cycloalkyl, heterocycloalkyl, haloalkyl, halocycloalkyl, or haloheterocycloalkyl;

15

wherein W is (C):

(C) is a six-membered heterocyclic ring system having 1-2 nitrogen atoms or a 10-membered bicyclic-six-six-fused-ring system having up to two nitrogen atoms within either or both rings, provided that no nitrogen is at a bridge of the bicyclic-six-six-fused-ring system, and further having 1-2 substituents independently selected
 20 from R_{C-1};

Each R_{C-1} is independently H, F, Cl, Br, I, alkyl, haloalkyl, substituted alkyl, alkenyl, haloalkenyl, substituted alkenyl, alkynyl, haloalkynyl, substituted alkynyl, cycloalkyl, halocycloalkyl, substituted cycloalkyl, heterocycloalkyl,
 25 haloheterocycloalkyl, substituted heterocycloalkyl, lactam heterocycloalkyl, phenyl, substituted phenyl, -NO₂, -CN, -OR_{C-2}, -SR_{C-2}, -SOR_{C-2}, -SO₂R_{C-2}, -NR_{C-2}C(O)R_{C-3}, -NR_{C-2}C(O)R_{C-2}, -NR_{C-2}C(O)R_{C-4}, -N(R_{C-2})₂, -C(O)R_{C-2}, -C(O)₂R_{C-2}, -C(O)N(R_{C-2})₂, -SCN, -NR_{C-2}C(O)R_{C-2}, -S(O)N(R_{C-2})₂, -S(O)₂N(R_{C-2})₂, -NR_{C-2}S(O)₂R_{C-2}, R₅, or R₆;

Each R_{C-2} is independently H, alkyl, cycloalkyl, heterocycloalkyl, alkyl
 30 substituted with 1 substituent selected from R_{C-5}, cycloalkyl substituted with 1 substituent selected from R_{C-5}, heterocycloalkyl substituted with 1 substituent selected from R_{C-5}, haloalkyl, halocycloalkyl, haloheterocycloalkyl, phenyl, or substituted phenyl;

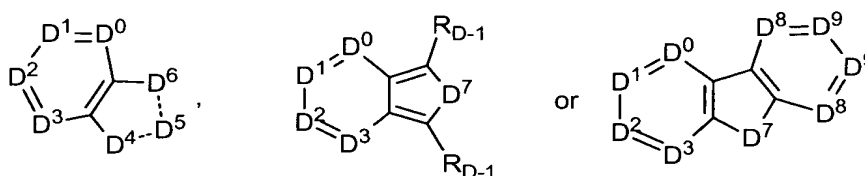
Each R_{C-3} is independently H, alkyl, or substituted alkyl;

R_{C-4} is H, alkyl, an amino protecting group, or an alkyl group having 1-3 substituents selected from F, Cl, Br, I, -OH, -CN, -NH₂, -NH(alkyl), or -N(alkyl)₂;

R_{C-5} is -CN, -CF₃, -NO₂, -OR_{C-6}, -SR_{C-6}, -N(R_{C-6})₂, -C(O)R_{C-6}, -SOR_{C-6},
 5 -SO₂RR_{C-6}, -C(O)N(R_{C-6})₂, -NR_{C-6}C(O)R_{C-6}, -S(O)₂N(R_{C-6})₂, or -NR_{C-6}S(O)₂R_{C-6};

Each R_{C-6} is independently H, alkyl, cycloalkyl, heterocycloalkyl, haloalkyl, halocycloalkyl, or haloheterocycloalkyl;

wherein W is (D):



10

provided that the bond between the -C(=X)- group and the W group may be attached at any available carbon atom within the D group as provided in R_{D-1} , R_{D-3} , and R_{D-4} ;

D^0 , D^1 , D^2 , and D^3 are N or C(R_{D-1}) provided that up to one of D^0 , D^1 , D^2 , or D^3 is N and the others are C(R_{D-1}), further provided that when the core molecule is
 15 attached at D^2 and D^0 or D^1 is N, D^3 is C(H), and further provided that there is only one attachment to the core molecule;

D^4 --- D^5 --- D^6 is selected from N(R_{D-2})-C(R_{D-3})=C(R_{D-3}), N=C(R_{D-3})-C(R_{D-4})₂,
 C(R_{D-3})=C(R_{D-3})-N(R_{D-2}), C(R_{D-3})₂-N(R_{D-2})-C(R_{D-3})₂, C(R_{D-4})₂-C(R_{D-3})=N,
 N(R_{D-2})-C(R_{D-3})₂-C(R_{D-3})₂, C(R_{D-3})₂-C(R_{D-3})₂-N(R_{D-2}), O-C(R_{D-3})=C(R_{D-3}),
 20 O-C(R_{D-3})₂-C(R_{D-3})₂, C(R_{D-3})₂-O-C(R_{D-3})₂, C(R_{D-3})=C(R_{D-3})-O, C(R_{D-3})₂-C(R_{D-3})₂-O,
 S-C(R_{D-3})=C(R_{D-3}), S-C(R_{D-3})₂-C(R_{D-3})₂, C(R_{D-3})₂-S-C(R_{D-3})₂, C(R_{D-3})=C(R_{D-3})-S,
 or C(R_{D-3})₂-C(R_{D-3})₂-S;

provided that when C(X) is attached to W at D^2 and D^6 is O, N(R_{D-2}), or S,
 D^4 --- D^5 is not CH=CH;

and further provided that when C(X) is attached to W at D^2 and D^4 is O,
 25 N(R_{D-2}), or S, D^5 --- D^6 is not CH=CH;

Each R_{D-1} is independently H, F, Br, I, Cl, -CN, -CF₃, -OR_{D-5}, -SR_{D-5},
 -N(R_{D-5})₂, or a bond to -C(X)- provided that only one of R_{D-1} , R_{D-3} , and R_{D-4} is said
 bond;

Each R_{D-2} is independently H, alkyl, haloalkyl, substituted alkyl, cycloalkyl, halocycloalkyl, substituted cycloalkyl, heterocycloalkyl, haloheterocycloalkyl, substituted heterocycloalkyl, R_5 , or R_6 ;

Each R_{D-3} is independently H, F, Br, Cl, I, alkyl, substituted alkyl, haloalkyl, alkenyl, substituted alkenyl, haloalkenyl, alkynyl, substituted alkynyl, haloalkynyl, heterocycloalkyl, substituted heterocycloalkyl, lactam heterocycloalkyl, -CN, -NO₂, -OR_{D-10}, -C(O)N(R_{D-11})₂, -NR_{D-10}COR_{D-12}, -N(R_{D-10})₂, -SR_{D-10}, -S(O)₂R_{D-10}, -C(O)R_{D-12}, -CO₂R_{D-10}, aryl, R_5 , R_6 , a bond to -C(X)- provided that only one of R_{D-1} , R_{D-3} , and R_{D-4} is said bond;

Each R_{D-4} is independently H, F, Br, Cl, I, alkyl, substituted alkyl, haloalkyl, alkenyl, substituted alkenyl, haloalkenyl, alkynyl, substituted alkynyl, haloalkynyl, heterocycloalkyl, substituted heterocycloalkyl, lactam heterocycloalkyl, -CN, -NO₂, -OR_{D-10}, -C(O)N(R_{D-11})₂, -NR_{D-10}COR_{D-12}, -N(R_{D-11})₂, -SR_{D-10}, -CO₂R_{D-10}, aryl, R_5 , R_6 , a bond to -C(X)- provided that only one of R_{D-1} , R_{D-3} , and R_{D-4} is said bond;

Each R_{D-5} is independently H, C₁₋₃ alkyl, or C₂₋₄ alkenyl;

D^7 is O, S, or N(R_{D-2});

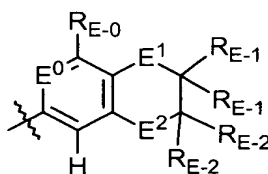
D^8 and D^9 are C(R_{D-1}), provided that when the molecule is attached to the phenyl moiety at D^9 , D^8 is CH;

Each R_{D-10} is H, alkyl, cycloalkyl, haloalkyl, substituted phenyl, or substituted naphthyl;

Each R_{D-11} is independently H, alkyl, cycloalkyl, heterocycloalkyl, alkyl substituted with 1 substituent selected from R_{13} , cycloalkyl substituted with 1 substituent selected from R_{13} , heterocycloalkyl substituted with 1 substituent selected from R_{13} , haloalkyl, halocycloalkyl, haloheterocycloalkyl, phenyl, or substituted phenyl;

R_{D-12} is H, alkyl, substituted alkyl, cycloalkyl, haloalkyl, heterocycloalkyl, substituted heterocycloalkyl, substituted phenyl, or substituted naphthyl;

wherein W is (E):



E^0 is CH or N;

R_{E-0} is H, F, Cl, Br, I, alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, haloalkyl, haloalkenyl, haloalkynyl, halocycloalkyl, haloheterocycloalkyl, substituted alkyl, substituted alkenyl, substituted alkynyl, substituted cycloalkyl, substituted heterocycloalkyl, aryl, R_5 , R_6 , $-OR_{E-3}$, $-OR_{E-4}$, $-SR_{E-3}$, $-SR_{E-5}$, $-N(R_{E-3})_2$, $-NR_{E-3}R_{E-6}$, $-N(R_{E-6})_2$, $-C(O)R_{E-3}$, $-CN$, $-C(O)N(R_{E-3})_2$, $-NR_{E-3}C(O)R_{E-3}$, $-S(O)R_{E-3}$, $-S(O)R_{E-5}$, $-OS(O)_2R_{E-3}$, $-NR_{E-3}S(O)_2R_{E-3}$, $-NO_2$, or $-N(H)C(O)N(H)R_{E-3}$;

E^1 is O, CR_{E-1-1} , or $C(R_{E-1-1})_2$, provided that when E^1 is CR_{E-1-1} , one R_{E-1} is a bond to CR_{E-1-1} , and further provided that at least one of E^1 or E^2 is O;

Each R_{E-1-1} is independently H, F, Br, Cl, CN, alkyl, haloalkyl, substituted alkyl, alkynyl, cycloalkyl, $-OR_E$, or $-N(R_E)_2$, provided that at least one R_{E-1-1} is H when E^1 is $C(R_{E-1-1})_2$;

Each R_{E-1} is independently H, alkyl, substituted alkyl, haloalkyl, cycloalkyl, heterocycloalkyl, or a bond to E^1 provided that E^1 is CR_{E-1-1} ;

E^2 is O, CR_{E-2-2} , or $C(R_{E-2-2})_2$, provided that when E^2 is CR_{E-2-2} , one R_{E-2} is a bond to CR_{E-2-2} , and further provided that at least one of E^1 or E^2 is O;

Each R_{E-2-2} is independently H, F, Br, Cl, CN, alkyl, haloalkyl, substituted alkyl, alkynyl, cycloalkyl, $-OR_E$, or $-N(R_E)_2$, provided that at least one R_{E-2-2} is H when E^2 is $C(R_{E-2-2})_2$;

Each R_{E-2} is independently H, alkyl, substituted alkyl, haloalkyl, cycloalkyl, heterocycloalkyl, or a bond to E^2 provided that E^2 is CR_{E-2-2} ;

Each R_E is independently H, alkyl, cycloalkyl, heterocycloalkyl, haloalkyl, halocycloalkyl, or haloheterocycloalkyl;

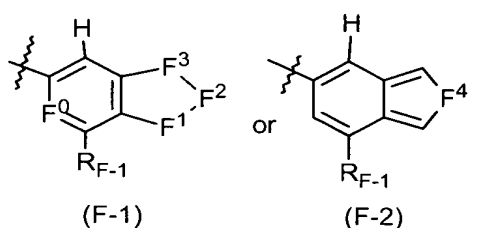
Each R_{E-3} is independently H, alkyl, haloalkyl, substituted alkyl, cycloalkyl, halocycloalkyl, substituted cycloalkyl, heterocycloalkyl, haloheterocycloalkyl, substituted heterocycloalkyl, R_5 , R_6 , phenyl, or phenyl having 1 substituent selected from R_9 and further having 0-3 substituents independently selected from F, Cl, Br, or I or substituted phenyl;

R_{E-4} is H, haloalkyl, substituted alkyl, cycloalkyl, halocycloalkyl, substituted cycloalkyl, heterocycloalkyl, haloheterocycloalkyl, substituted heterocycloalkyl, R_5 , R_6 , phenyl, or substituted phenyl;

Each R_{E-5} is independently H, haloalkyl, substituted alkyl, cycloalkyl, halocycloalkyl, substituted cycloalkyl, heterocycloalkyl, haloheterocycloalkyl, substituted heterocycloalkyl, R_5 , or R_6 ;

Each R_{E-6} is independently alkyl, haloalkyl, substituted alkyl, cycloalkyl, halocycloalkyl, substituted cycloalkyl, heterocycloalkyl, haloheterocycloalkyl, substituted heterocycloalkyl, R_5 , R_6 , phenyl, or phenyl having 1 substituent selected from R_9 and further having 0-3 substituents independently selected from F, Cl, Br, or I;

wherein W is (F):



F^0 is C(H) wherein $F^1\text{---}F^2\text{---}F^3$ is selected from O-C(R_{F-2})=N, O-C(R_{F-3})(R_{F-2})-N(R_{F-4}), O-C(R_{F-3})(R_{F-2})-S, O-N=C(R_{F-3}), O-C(R_{F-2})(R_{F-3})-O, S-C(R_{F-2})=N, S-C(R_{F-3})(R_{F-2})-N(R_{F-4}), S-N=C(R_{F-3}), N=C(R_{F-2})-O, N=C(R_{F-2})-S, N=C(R_{F-2})-N(R_{F-4}), N(R_{F-4})-N=C(R_{F-3}), N(R_{F-4})-C(R_{F-3})(R_{F-2})-O, N(R_{F-4})-C(R_{F-3})(R_{F-2})-S, N(R_{F-4})-C(R_{F-3})(R_{F-2})-N(R_{F-4}), C(R_{F-3})₂-O-N(R_{F-4}), C(R_{F-3})₂-N(R_{F-4})-O, C(R_{F-3})₂-N(R_{F-4})-S, C(R_{F-3})=N-O, C(R_{F-3})=N-S, C(R_{F-3})=N-N(R_{F-4}), or C(R_{F-3})₂-C(R_{F-2})(R_{F-3})-C(R_{F-3})₂;

F^0 is N wherein $F^1\text{---}F^2\text{---}F^3$ is selected from O-C(R_{F-2})=N, O-C(R_{F-3})(R_{F-2})-N(R_{F-4}), O-C(R_{F-3})(R_{F-2})-S, O-N=C(R_{F-3}), O-C(R_{F-2})(R_{F-3})-O, S-C(R_{F-2})=N, S-C(R_{F-3})(R_{F-2})-N(R_{F-4}), S-N=C(R_{F-3}), N=C(R_{F-2})-O, N=C(R_{F-2})-S, N=C(R_{F-2})-N(R_{F-4}), N(R_{F-4})-N=C(R_{F-3}), N(R_{F-4})-C(R_{F-3})(R_{F-2})-O, N(R_{F-4})-C(R_{F-3})(R_{F-2})-S, N(R_{F-4})-C(R_{F-3})(R_{F-2})-N(R_{F-4}), C(R_{F-3})₂-O-N(R_{F-4}), C(R_{F-3})₂-N(R_{F-4})-O, C(R_{F-3})₂-N(R_{F-4})-S, C(R_{F-3})=N-O, C(R_{F-3})=N-S, C(R_{F-3})=N-N(R_{F-4}), C(R_{F-3})=C(R_{F-2})-C(R_{F-3})₂, or C(R_{F-3})₂-C(R_{F-2})(R_{F-3})-C(R_{F-3})₂;

F^4 is N(R_{F-7}), O, or S;

R_{F-1} is H, F, Cl, Br, I, -CN, -CF₃, -OR_{F-8}, -SR_{F-8}, or -N(R_{F-8})₂;

R_{F-2} is H, F, alkyl, haloalkyl, substituted alkyl, lactam heterocycloalkyl, phenoxy, substituted phenoxy, R_5 , R_6 , -N(R_{F-4})-aryl,

-N(R_{F-4})-substituted phenyl, -N(R_{F-4})-substituted naphthyl, -O-substituted phenyl,

-O-substituted naphthyl, -S-substituted phenyl, -S-substituted naphthyl, or alkyl substituted on the ω carbon with R_{F-9} ;

R_{F-3} is H, F, Br, Cl, I, alkyl, substituted alkyl, haloalkyl, alkenyl, substituted alkenyl, haloalkenyl, alkynyl, substituted alkynyl, haloalkynyl, heterocycloalkyl, substituted heterocycloalkyl, lactam heterocycloalkyl, -CN, -NO₂, -OR_{F-8},
 5 -C(O)N(R_{F-8})₂, -NHR_{F-8}, -NR_{F-8}COR_{F-8}, -N(R_{F-8})₂, -SR_{F-8}, -C(O)R_{F-8}, -CO₂R_{F-8}, aryl, R₅, or R₆;

R_{F-4} is H, or alkyl;

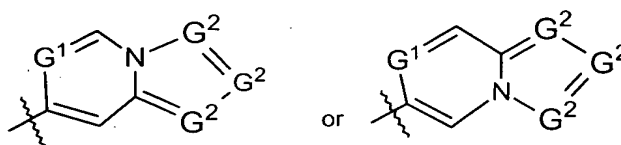
R_{F-7} is H, alkyl, haloalkyl, substituted alkyl, cycloalkyl, halocycloalkyl, substituted cycloalkyl, phenyl, or phenyl having 1 substituent selected from R₉ and
 10 further having 0-3 substituents independently selected from F, Cl, Br, or I;

R_{F-8} is H, alkyl, substituted alkyl, cycloalkyl, haloalkyl, heterocycloalkyl, substituted heterocycloalkyl, substituted phenyl, or substituted naphthyl;

R_{F-9} is aryl, R₅, or R₆;

15

wherein W is (G):



G^1 is N or CH;

Each G^2 is N or C(R_{G-1}), provided that no more than one G^2 N;

Each R_{G-1} is independently H, alkyl, substituted alkyl, haloalkyl, alkenyl, substituted alkenyl, haloalkenyl, alkynyl, substituted alkynyl, haloalkynyl, -CN, -NO₂,
 20 F, Br, Cl, I, -C(O)N(R_{G-3})₂, -N(R_{G-3})₂, -SR_{G-6}, -S(O)₂R_{G-6}, -OR_{G-6}, -C(O)R_{G-6}, -CO₂R_{G-6}, aryl, R₅, R₆, or two R_{G-1} on adjacent carbon atoms may combine for W to be a 6-5-6 fused-tricyclic-heteroaromatic-ring system optionally substituted on the
 25 newly formed ring where valency allows with 1-2 substituents independently selected from F, Cl, Br, I, and R_{G-2};

R_{G-2} is alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, haloalkyl, haloalkenyl, haloalkynyl, halocycloalkyl, haloheterocycloalkyl, -OR_{G-8}, -SR_{G-8},
 -S(O)₂R_{G-8}, -S(O)R_{G-8}, -OS(O)₂R_{G-8}, -N(R_{G-8})₂, -C(O)R_{G-8}, -C(S)R_{G-8}, -C(O)OR_{G-8},
 30 -CN, -C(O)N(R_{G-8})₂, -NR_{G-8}C(O)R_{G-8}, -S(O)₂N(R_{G-8})₂, -NR_{G-8}S(O)₂R_{G-8}, -NO₂,

-N(R_{G-8})C(O)N(R_{G-8})₂, substituted alkyl, substituted alkenyl, substituted alkynyl, substituted cycloalkyl, substituted heterocycloalkyl, lactam heterocycloalkyl, phenyl, phenyl having 0-4 substituents independently selected from F, Cl, Br, I and R_{G-7}, naphthyl, or naphthyl having 0-4 substituents independently selected from F, Cl, Br, I,
 5 or R_{G-7};

provided that when G² adjacent to the bridge N is C(R_{G-1}) and the other G² are CH, that R_{G-1} is other than H, F, Cl, I, alkyl, substituted alkyl or alkynyl;

Each R_{G-3} is independently H, alkyl, cycloalkyl, heterocycloalkyl, alkyl substituted with 1 substituent selected from R_{G-4}, cycloalkyl substituted with 1
 10 substituent selected from R_{G-4}, heterocycloalkyl substituted with 1 substituent selected from R_{G-4}, haloalkyl, halocycloalkyl, haloheterocycloalkyl, phenyl, or substituted phenyl;

R_{G-4} is -OR_{G-5}, -SR_{G-5}, -N(R_{G-5})₂, -C(O)R_{G-5}, -SOR_{G-5}, -SO₂R_{G-5}, -C(O)N(R_{G-5})₂, -CN, -CF₃, -NR_{G-5}C(O)R_{G-5}, -S(O)₂N(R_{G-5})₂, -NR_{G-5}S(O)₂R_{G-5}, or
 15 -NO₂;

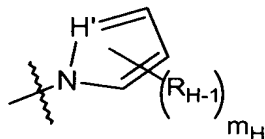
Each R_{G-5} is independently H, alkyl, cycloalkyl, heterocycloalkyl, haloalkyl, halocycloalkyl, or haloheterocycloalkyl;

R_{G-6} is H, alkyl, haloalkyl, substituted alkyl, cycloalkyl, halocycloalkyl, substituted cycloalkyl, phenyl, or phenyl having 0-4 substituents independently
 20 selected from F, Cl, Br, I, and R_{G-7};

R_{G-7} is alkyl, substituted alkyl, haloalkyl, -OR_{G-5}, -CN, -NO₂, -N(R_{G-3})₂;

Each R_{G-8} is independently H, alkyl, haloalkyl, substituted alkyl, cycloalkyl, halocycloalkyl, substituted cycloalkyl, heterocycloalkyl, haloheterocycloalkyl, substituted heterocycloalkyl, phenyl, or phenyl substituted with 0-4 independently
 25 selected from F, Cl, Br, I, or R_{G-7};

wherein W is (H)



H' is N or CH;

Each R_{H-1} is independently F, Cl, Br, I, -CN, -NO₂, alkyl, haloalkyl, substituted alkyl, alkenyl, haloalkenyl, substituted alkenyl, alkynyl, haloalkynyl,
 30

substituted alkynyl, cycloalkyl, halocycloalkyl, substituted cycloalkyl, heterocycloalkyl, haloheterocycloalkyl, substituted heterocycloalkyl, lactam heterocycloalkyl, aryl, R_5 , R_6 , $-OR_8$, $-SR_8$, $-SOR_8$, $-SO_2R_8$, $-SCN$, $-S(O)N(R_8)_2$, $-S(O)_2N(R_8)_2$, $-C(O)R_8$, $-C(O)_2R_8$, $-C(O)N(R_8)_2$, $C(R_8)=N-OR_8$, $-NC(O)R_5$,
 5 $-NC(O)R_{H-3}$, $-NC(O)R_6$, $-N(R_8)_2$, $-NR_8C(O)R_8$, $-NR_8S(O)_2R_8$, or two R_{H-1} on adjacent carbon atoms may fuse to form a 6-membered ring to give a 5-6 fused, bicyclic moiety where the 6-membered ring is optionally substituted with 1-3 substituents selected from R_{H-2} ;

m_H is 0, 1, or 2;

10 R_{H-2} is alkyl, alkenyl, alkynyl, cycloalkyl, heterocycloalkyl, haloalkyl, haloalkenyl, haloalkynyl, halocycloalkyl, haloheterocycloalkyl, $-OR_{H-3}$, $-SR_{H-3}$, $-S(O)_2R_{H-3}$, $-S(O)R_{H-3}$, $-OS(O)_2R_{H-3}$, $-N(R_{H-3})_2$, $-C(O)R_{H-3}$, $-C(S)R_{H-3}$, $-C(O)OR_{H-3}$, $-CN$, $-C(O)N(R_{H-3})_2$, $-NR_{H-3}C(O)R_{H-3}$, $-S(O)_2N(R_{H-3})_2$, $-NR_{H-3}S(O)_2R_{H-3}$, $-NO_2$, $-N(R_{H-3})C(O)N(R_{H-3})_2$, substituted alkyl, substituted alkenyl, substituted alkynyl,
 15 substituted cycloalkyl, substituted heterocycloalkyl, lactam heterocycloalkyl, phenyl, phenyl having 0-4 substituents independently selected from F, Cl, Br, I and R_7 , naphthyl, naphthyl having 0-4 substituents independently selected from F, Cl, Br, I, or R_7 , or two R_{H-2} on adjacent carbon atoms may combine to form a three-ring-fused-5-6-6 system optionally substituted with up to 3 substituents independently selected
 20 from Br, Cl, F, I, $-CN$, $-NO_2$, $-CF_3$, $-N(R_{H-3})_2$, $-N(R_{H-3})C(O)R_{H-3}$, alkyl, alkenyl, and alkynyl;

Each R_{H-3} is independently H, alkyl, haloalkyl, substituted alkyl, cycloalkyl, halocycloalkyl, substituted cycloalkyl, heterocycloalkyl, haloheterocycloalkyl, substituted heterocycloalkyl, phenyl, or phenyl substituted with 0-4 independently
 25 selected from F, Cl, Br, I, or R_7 ;

or pharmaceutical composition, pharmaceutically acceptable salt, racemic mixture, or pure enantiomer thereof.

18. The composition of claim 17, wherein X is O, R_1 is H, R_2 is absent, R_{2-3} is H,
 30 each R_3 is H, R_4 is H and W is 4-chlorobenz-1-yl; dibenzo[b,d]thiophene-2-yl; isoquinoline-3-yl; furo[2,3-c]pyridine-5-yl; 1,3-benzodioxole-5-yl; 2,3-dihydro-1,4-benzodioxine-6-yl; 1,3-benzoxazole-5-yl; thieno[2,3-c]pyridine-5-yl; thieno[3,2-c]pyridine-6-yl; [1]benzothieno[3,2-c]pyridine-3-yl; 1,3-benzothiazole-6-yl;

thieno[3,4-c]pyridine-6-yl; 2,3-dihydro-1-benzofuran-5-yl; 1-benzofuran-5-yl;
 furo[3,2-c]pyridine-6-yl; [1]benzothieno[2,3-c]pyridine-3-yl; dibenzo[b,d]furan-2-yl;
 1-benzofuran-6-yl; 2-naphthyl; 1H-indole-6-yl; pyrrolo[1,2-c]pyrimidine-3-yl; 1-
 benzothiophene-5-yl; 1-benzothiophene-5-yl; 1-benzothiophene-6-yl; pyrrolo[1,2-
 5 a]pyrazine-3-yl; 1H-indole-6-yl; pyrazino[1,2-a]indole-3-yl; 1,3-benzothiazole-6-yl;
 [1]benzofuro[2,3-c]pyridine-3-yl; [1]benzofuro[2,3-c]pyridine-3-yl; 2H-chromene-6-
 yl; indolizine-6-yl; and [1,3]dioxolo[4,5-c]pyridine-6-yl; any of which is optionally
 substituted as allowed in claim 17.

- 10 19. The composition of claim 18, wherein the agonist is
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-4-chlorobenzamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]dibenzo[b,d]thiophene-2-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]isoquinoline-3-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]furo[2,3-c]pyridine-5-carboxamide;
 15 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-1,3-benzodioxole-5-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-2-methylfuro[2,3-c]pyridine-5-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-2,3-dihydro-1,4-benzodioxine-6-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-3-methylfuro[2,3-c]pyridine-5-carboxamide;
 N-[(1S,2R,4R)-7-azabicyclo[2.2.1]hept-2-yl]isoquinoline-3-carboxamide;
 20 N-[(1S,2R,4R)-7-azabicyclo[2.2.1]hept-2-yl]-3-methylfuro[2,3-c]pyridine-5-
 carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-1,3-benzoxazole-5-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-2-methyl-1,3-benzoxazole-5-carboxamide;
 N-[(1S,2R,4R)-7-azabicyclo[2.2.1]hept-2-yl]thieno[2,3-c]pyridine-5-carboxamide;
 25 N-[(1S,2R,4R)-7-azabicyclo[2.2.1]hept-2-yl]thieno[3,2-c]pyridine-6-carboxamide;
 N-[(1S,2R,4R)-7-azabicyclo[2.2.1]hept-2-yl]furo[2,3-c]pyridine-5-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-3-ethylfuro[2,3-c]pyridine-5-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-3-isopropylfuro[2,3-c]pyridine-5-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]thieno[2,3-c]pyridine-5-carboxamide;
 30 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]thieno[3,2-c]pyridine-6-carboxamide;
 5-{[(2R)-7-azoniabicyclo[2.2.1]hept-2-ylamino]carbonyl}-3-ethylfuro[2,3-c]pyridin-
 6-ium dichloride;

- 5-{[(2R)-7-azoniabicyclo[2.2.1]hept-2-ylamino]carbonyl}-3-isopropylfuro[2,3-c]pyridin-6-ium dichloride;
- N-[(3R,4S)-1-azabicyclo[2.2.1]hept-3-yl]furo[2,3-c]pyridine-5-carboxamide;
- N-1-azabicyclo[2.2.2]oct-3-yl[1]benzothieno[3,2-c]pyridine-3-carboxamide;
- 5 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-1,3-benzothiazole-6-carboxamide;
- N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-3-chlorofuro[2,3-c]pyridine-5-carboxamide;
- N-1-azabicyclo[2.2.2]oct-3-ylfuro[2,3-c]pyridine-5-carboxamide;
- N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]thieno[3,4-c]pyridine-6-carboxamide;
- N-[(3R,5R)-1-azabicyclo[3.2.1]oct-3-yl]-3-methylfuro[2,3-c]pyridine-5-carboxamide;
- 10 N-[(3R,4S)-1-azabicyclo[2.2.1]hept-3-yl]-3-methylfuro[2,3-c]pyridine-5-carboxamide;
- N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-2,3-dihydro-1-benzofuran-5-carboxamide;
- N-[(3R,4S)-1-azabicyclo[2.2.1]hept-3-yl]thieno[2,3-c]pyridine-5-carboxamide;
- N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-1-benzofuran-5-carboxamide;
- 15 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]furo[3,2-c]pyridine-6-carboxamide;
- N-[(3R,4S)-1-azabicyclo[2.2.1]hept-3-yl]thieno[3,2-c]pyridine-6-carboxamide;
- N-[(3R,4S)-1-azabicyclo[2.2.1]hept-3-yl]3-ethylfuro[2,3-c]pyridine-5-carboxamide;
- N-[(3R,4S)-1-azabicyclo[2.2.1]hept-3-yl]3-isopropylfuro[2,3-c]pyridine-5-carboxamide;
- 20 N-[(1S,2R,4R)-7-azabicyclo[2.2.1]hept-2-yl]-3-chlorofuro[2,3-c]pyridine-5-carboxamide;
- N-[(3R,4S)-1-azabicyclo[2.2.1]hept-3-yl]3-chlorofuro[2,3-c]pyridine-5-carboxamide;
- N-[(2S,3R)-2-methyl-1-azabicyclo[2.2.2]oct-3-yl]furo[2,3-c]pyridine-5-carboxamide;
- N-[(3R,5R)-1-azabicyclo[3.2.1]oct-3-yl]-4-chlorobenzamide;
- 25 N-[(1S,2R,4R)-7-azabicyclo[2.2.1]hept-2-yl]thieno[3,4-c]pyridine-6-carboxamide;
- N-[(1S,2R,4R)-7-azabicyclo[2.2.1]hept-2-yl]dibenzo[b,d]thiophene-2-carboxamide;
- N-[(3R,4S)-1-azabicyclo[2.2.1]hept-3-yl]-1-benzofuran-5-carboxamide;
- N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl][1]benzothieno[2,3-c]pyridine-3-carboxamide;
- N-[(1S,2R,4R)-7-azabicyclo[2.2.1]hept-2-yl][1]benzothieno[2,3-c]pyridine-3-
- 30 carboxamide;
- N-[(1S,2R,4R)-7-azabicyclo[2.2.1]hept-2-yl]-1-benzofuran-5-carboxamide;
- N-[(1S,2R,4R)-7-azabicyclo[2.2.1]hept-2-yl]dibenzo[b,d]furan-2-carboxamide;
- N-[(3R,5R)-1-azabicyclo[3.2.1]oct-3-yl]furo[2,3-c]pyridine-5-carboxamide;

- N-[(3R,5R)-1-azabicyclo[3.2.1]oct-3-yl]furo[2,3-c]pyridine-5-carboxamide;
 N-[(3R,5R)-1-azabicyclo[3.2.1]oct-3-yl]-1-benzofuran-5-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-3-bromofuro[2,3-c]pyridine-5-carboxamide;
 N-[(1S,2R,4R)-7-azabicyclo[2.2.1]hept-2-yl]-3-bromofuro[2,3-c]pyridine-5-
 5 carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-1-benzofuran-6-carboxamide;
 N-[(2S,3R)-2-methyl-1-azabicyclo[2.2.2]oct-3-yl]-2-naphthamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]pyrrolo[1,2-c]pyrimidine-3-carboxamide;
 N-[(3R,5R)-1-azabicyclo[3.2.1]oct-3-yl]thieno[2,3-c]pyridine-5-carboxamide;
 10 N-[(3R,5R)-1-azabicyclo[3.2.1]oct-3-yl]thieno[3,2-c]pyridine-6-carboxamide;
 N-[(2S,3R)-2-methyl-1-azabicyclo[2.2.2]oct-3-yl]furo[2,3-c]pyridine-5-carboxamide;
 N-[(3R,4S)-1-azabicyclo[2.2.1]hept-3-yl]-1H-indole-6-carboxamide;
 N-[(2S,3R)-2-methyl-1-azabicyclo[2.2.2]oct-3-yl]thieno[2,3-c]pyridine-5-
 carboxamide;
 15 3-methyl-N-[(2S,3R)-2-methyl-1-azabicyclo[2.2.2]oct-3-yl]furo[2,3-c]pyridine-5-
 carboxamide;
 N-[(2S,3R)-2-methyl-1-azabicyclo[2.2.2]oct-3-yl]-1-benzofuran-5-carboxamide;
 N-[(2S,3R)-2-methyl-1-azabicyclo[2.2.2]oct-3-yl]thieno[3,2-c]pyridine-6-
 carboxamide;
 20 N-[(2S,3R)-2-methyl-1-azabicyclo[2.2.2]oct-3-yl]pyrrolo[1,2-c]pyrimidine-3-
 carboxamide;
 N-[(2S,3R)-2-methyl-1-azabicyclo[2.2.2]oct-3-yl]-1,3-benzothiazole-6-carboxamide;
 N-[(3R,5R)-1-azabicyclo[3.2.1]oct-3-yl]pyrrolo[1,2-c]pyrimidine-3-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-1-benzothiophene-5-carboxamide;
 25 N-[(1S,2R,4R)-7-azabicyclo[2.2.1]hept-2-yl]pyrrolo[1,2-c]pyrimidine-3-carboxamide;
 N-[(3R,4S)-1-azabicyclo[2.2.1]hept-3-yl]pyrrolo[1,2-c]pyrimidine-3-carboxamide;
 N-[(3R,4S)-1-azabicyclo[2.2.1]hept-3-yl]-3-bromofuro[2,3-c]pyridine-5-carboxamide;
 N-[(3R,4S)-1-azabicyclo[2.2.1]hept-3-yl]-1,3-benzodioxole-5-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-3-bromo-1-benzofuran-5-carboxamide;
 30 N-[(1S,2R,4R)-7-azabicyclo[2.2.1]hept-2-yl]-3-bromo-1-benzofuran-5-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-3-bromothieno[2,3-c]pyridine-5-carboxamide;
 N-[(1S,2R,4R)-7-azabicyclo[2.2.1]hept-2-yl]-3-bromothieno[2,3-c]pyridine-5-
 carboxamide;

- N-[(3R,4S)-1-azabicyclo[2.2.1]hept-3-yl]-1-benzothiophene-5-carboxamide;
 N-[(3S)-1-azabicyclo[2.2.2]oct-3-yl]furo[2,3-c]pyridine-5-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-3-methyl-1-benzofuran-5-carboxamide;
 N-[(1S,2R,4R)-7-azabicyclo[2.2.1]hept-2-yl]-3-methyl-1-benzofuran-5-carboxamide;
 5 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-2-methyl-1-benzofuran-6-carboxamide;
 N-[(3R,5R)-1-azabicyclo[3.2.1]oct-3-yl]-1-benzofuran-6-carboxamide;
 N-[(2S,3R)-2-methyl-1-azabicyclo[2.2.2]oct-3-yl]-1-benzofuran-6-carboxamide;
 N-[(2S,3R)-2-methyl-1-azabicyclo[2.2.2]oct-3-yl]-1-benzothiophene-5-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-1-benzothiophene-6-carboxamide;
 10 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]pyrrolo[1,2-a]pyrazine-3-carboxamide;
 N-[(3R,4S)-1-azabicyclo[2.2.1]hept-3-yl]-1-benzothiophene-6-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-1-methyl-1H-indole-6-carboxamide;
 N-[(3S)-1-azabicyclo[2.2.2]oct-3-yl]-1-benzofuran-5-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-3-isopropyl-1-benzofuran-5-carboxamide;
 15 N-[(1S,2R,4R)-7-azabicyclo[2.2.1]hept-2-yl]-3-isopropyl-1-benzofuran-5-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-3-ethynylfuro[2,3-c]pyridine-5-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-1H-indazole-6-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-2-methyl-1-benzofuran-5-carboxamide;
 20 N-[(1S,2R,4R)-7-azabicyclo[2.2.1]hept-2-yl]-2-methyl-1-benzofuran-5-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]pyrazino[1,2-a]indole-3-carboxamide;
 3-bromo-N-[(2S,3R)-2-methyl-1-azabicyclo[2.2.2]oct-3-yl]furo[2,3-c]pyridine-5-carboxamide;
 N-[(3R,5R)-1-azabicyclo[3.2.1]oct-3-yl]pyrrolo[1,2-a]pyrazine-3-carboxamide;
 25 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-7-methoxy-2-naphthamide;
 N-[(1S,2R,4R)-7-azabicyclo[2.2.1]hept-2-yl]pyrrolo[1,2-a]pyrazine-3-carboxamide;
 N-[(3R,5R)-1-azabicyclo[3.2.1]oct-3-yl]-1,3-benzothiazole-6-carboxamide;
 N-[(3R,4S)-1-azabicyclo[2.2.1]hept-3-yl]-3-bromo-1-benzofuran-6-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl][1]benzofuro[2,3-c]pyridine-3-carboxamide;
 30 N-[(1S,2R,4R)-7-azabicyclo[2.2.1]hept-2-yl][1]benzofuro[2,3-c]pyridine-3-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-3-ethynyl-1-benzofuran-5-carboxamide;
 N-[(1S,2R,4R)-7-azabicyclo[2.2.1]hept-2-yl]-3-ethynyl-1-benzofuran-5-carboxamide;

- N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-2H-chromene-6-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-3-prop-1-ynyl-1-benzofuran-5-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-2-phenyl-1,3-benzodioxole-5-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-6-bromopyrrolo[1,2-a]pyrazine-3-carboxamide;
 5 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-3-prop-1-ynylfuro[2,3-c]pyridine-5-carboxamide;
 N-[(2S,3R)-2-methyl-1-azabicyclo[2.2.2]oct-3-yl]pyrrolo[1,2-a]pyrazine-3-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]indolizine-6-carboxamide;
 10 2-amino-N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-1,3-benzothiazole-6-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-6-ethynylpyrrolo[1,2-a]pyrazine-3-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-8-methoxy-2-naphthamide;
 N-[(2S,3R)-2-methyl-1-azabicyclo[2.2.2]oct-3-yl]indolizine-6-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl][1,3]dioxolo[4,5-c]pyridine-6-carboxamide;
 15 N-[(1S,2R,4R)-7-azabicyclo[2.2.1]hept-2-yl][1,3]dioxolo[4,5-c]pyridine-6-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-3-cyano-1-benzofuran-5-carboxamide;
 N-[(3R,4S)-1-azabicyclo[2.2.1]hept-3-yl][1,3]dioxolo[4,5-c]pyridine-6-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-3-ethyl-2,3-dihydro-1,4-benzodioxine-6-
 20 carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-7-hydroxy-2-naphthamide;
 N-[(1S,2R,4R)-7-azabicyclo[2.2.1]hept-2-yl]-3-ethynylfuro[2,3-c]pyridine-5-carboxamide;
 N-[(1S,2R,4R)-7-azabicyclo[2.2.1]hept-2-yl]-6-chloroisoquinoline-3-carboxamide;
 25 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-3-ethyl-2,3-dihydro-1,4-benzodioxine-6-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-3-ethyl-2,3-dihydro-1,4-benzodioxine-6-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-6-methylisoquinoline-3-carboxamide;
 30 N-[(1S,2R,4R)-7-azabicyclo[2.2.1]hept-2-yl]-6-methylisoquinoline-3-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-3-cyanofuro[2,3-c]pyridine-5-carboxamide;
 N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]-2-naphthamide; and

N-[(3R)-1-azabicyclo[2.2.2]oct-3-yl]dibenzo[b,d]furan-2-carboxamide, provided that the agonist is a free base or a pharmaceutically acceptable salt thereof.

20. The composition of claim 19, wherein the Acetylcholinesterase inhibitor is
- 5 physostigmine, aricept, rivastigmine, galantamine, monoamine acridines and derivatives, piperidinyl-alkanoyl heterocyclic compounds, N-benzyl-piperidine derivatives, 4-(1-benzylpiperidyl)-substituted fused quinoline derivatives, and cyclic amide derivatives.